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VACCINE THERAPY IN GENERAL PRACTICE

BY

G. H. SHERMAN, M. D.

Also Quotations from Other Authors

THIRD EDITION

Published by
G. H. SHERMAN, M. D.
Detroit, Mich.
1916

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PREFACE TO THE THIRD EDITION

The underlying basis for further development in progressive medicine depends upon accurate interpretation of scientific investigations. In considering the progress of Vaccine Therapy and its important contributions to the science of medicine, all elements that enter into its development should be ascertained and the principles pertaining to its application recognized.

This book, as its title indicates, is meant for the physician in active practice. No attempt is herein made to enter into a minute description of bacteriological laboratory procedures, or to detail the complex phases of bacteriopathology. My aim is to present scientific observations on vaccine therapy which are of value in the treatment of infectious diseases met in every day practice. Accordingly, it records in concentrated form my experience with Immunotherapy (bacterial vaccines), supplemented by much data, drawn from publications dealing with this subject. The first part of the volume reviews briefly the underlying principles of vaccine therapy, the remainder is devoted to a discussion of its indications, limitations and applications.

The first edition of Vaccine Therapy in General Practice was produced at the request of many friends, and was intended to serve as an easy means of answering questions which were continually being brought up; it was an effort to educate the profession to a better, more comprehensive knowledge of vaccine therapy. Then a second edition was called for and well received, which gives me the great personal gratification of feeling that in some measure at least, I have contributed to a growing knowledge and appreciation of what I believe to be as important in medicine as antisepsis is in surgery.

I hope that this third edition will serve a still better purpose. Much additional knowledge has accumulated during the past few years, greatly extending the scope of therapeutic and prophylactic immunization which necessitates a much more extensive presentation of the subject. The book has been entirely rewritten and the chapters which deal specially on the treatment of diseases have been rearranged to make the subjects under consideration conform, as nearly as possible, to infections of the different parts of the body that perform certain functions. By this arrangement, specialists may readily refer to the subject in which they are mostly interested.

Those who have a personal knowledge of the value of vaccine therapy, need no more evidence that it has attained a permanent place in modern therapeutics. To those who have hesitated to form a personal acquaintance with it, perhaps purely on account of academic pronouncements, or, because of a vague fear unfortunately brought on by prejudice, I would say that progress and development, in all branches of scientific medicine, is possible only by applying facts impartially and by discarding all obstructing elements. This is essential to the advancement of knowledge. Deductions as to scientific interpretation of facts cannot be based upon prejudice and academic speculations. In this regard, I earnestly offer the words of Huxley: "Sit down before a fact like a little child; be prepared to give up every preconceived notion; follow it humbly, wherever it may lead you or you shall learn nothing."

Marked success in any endeavor is liable to make one over-enthusiastic. Realizing this, I have been very careful not to make over-statements. Extensive vaccine users criticise me as being too conservative,

In my extracts from publications by other authors, extensive quotations are frequently made use of, for the purpose of conveying the exact ideas of the authors. Abstracts were, in many instances, unavoidable for the want of space, but in making them, the thought of the author is presented as clearly as possible.

It is entirely proper that I should acknowledge my sense of obligation to the many authors from whose works I have so liberally drawn, and thanks are also due to many doctors who have voluntarily given experiences with the use of bacterial vaccines which so materially aided me in obtaining information on a larger scale.

I also wish to extend thanks to my assistants in the laboratory, for their aid in making much of this extensive work possible.

G. H. S.

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CHAPTER I.

THE PHILOSOPHY OF VACCINE THERAPY.

That many diseases are communicable, and that in certain diseases one attack renders the individual subsequently immune, has been known since the dawn of medicine; but it was left to our generation, through the development of the science of bacteriology, to ascertain the causes of transmitted disease and the nature of the immunizing mechanism. Bacteriology has demonstrated that a surprisingly large proportion of our diseases are caused by the ever-present germs and that health is maintained only by the workings of the defense organs against the attacks of pathogenic bacteria. The basic principle of vaccine therapy is this production of immunity, and its aim is to take advantage of nature's immunizing methods and to utilize them for prophylactic and curative purposes.

Antibacterial Substances of the Blood.

Extensive research work on lower animals by numerous investigators has quite accurately determined the presence of antibacterial substances in the blood. Buchner, Nutall and others found that fresh normal blood serum has a bactericidal power, dissolving to a limited extent many kinds of germs. Park showed that as many as 30,000 germs per cubic centimeter of fluid will all be destroyed by 0.1 c.c. of normal blood serum incubated at 98.1 degrees F. for 27 hours. When 100,000 germs are added to the same amount of serum the number of germs will be very much diminished during the first and second hours of incubation, but if the process of incubation is continued for 27 hours, the number of germs is materially increased, the remaining live germs having multiplied. This shows that

normal blood serum contains a substance that is consumed while destroying germs, and that if there be any germs left after this substance is consumed they will at once multiply without further hindrance.

Ehrlich and Morgenroth found that this bactericidal power of fresh blood serum is due to the presence, in very minute quantities, of a variety of substances, termed antibodies, which combine with another substance called the complement, present in comparatively large amounts. These antibodies fit a large variety of organisms, but when an animal is immunized to some specific organism the antibodies corresponding to that organism are enormously increased, while the amount of complement present remains practically stationary.

Since the germ-destroying power of the blood depends on the combination of the antibodies with the complement, it can readily be seen that in cases of advanced infections the immunizing process may be retarded from a deficiency in complement.

Longcope (University of Penn. Med. Bulletin, 1902, XV, 331), in an investigation of the complement-content of the blood in infectious diseases in general, has found that the complement is constantly low, and is diminished still more when septic complications intervene.

Gay, Perkins, Thompson (Jour. Med. Research, 1903, X, 196) found a diminished bacteriolytic complement constant in variola. Wasserman suggested ("Immune Sera," by C. F. Bolduan, 1911, p. 81) that the curative power of many bactericidal sera might be increased by the simultaneous injection of the sera of certain normal animals in order thus to gain an increased amount of complement.

In infections caused by exotoxic organisms such as the diphtheria and tetanus bacilli, distinct antitoxins are formed as the principal immunizing factors. In the infections

caused by the endotoxic pus group of organisms, of which the streptococci, pneumococci, staphylococci, colon bacilli, and typhoid bacilli are the most important, the immune body or amboceptor expresses itself in the form of agglutinins, lysins, precipitins, etc.

Metchnikoff found that the white corpuscles play an important role in the immunizing process as phagocytes or "devouring cells," having the power to take up germs and destroy them by a process of digestion.

THE OPSONINS.

Sir A. E. Wright, of London, following up Metchnikoff's work, found that the phagocytic power of the white corpuscles was very low or almost entirely negative unless they were suspended in blood serum, and that when the corpuscles are suspended in blood serum obtained from previously immunized animals their phagocytic power is much greater than when they are suspended in ordinary serum. He also found that this phagocytic power is specific, it only appearing when the same kind of germs that the animal was immunized with are used in the experiment. This is the fundamental principle of this subject.

From these investigations Wright concluded that the blood serum contains a substance which has a sensitizing effect on the invading organism and that this substance is naturally increased during the immunizing process. This bacteriotropic substance he termed opsonin (Greek, Opsono, I prepare food for). It was this phagocytic power of the blood as demonstrated in the incubated test tube that led Wright to make extensive investigations as to the opsonic power of the blood in man under various conditions. A measurement of this power he calls the "opsonic index," and he obtains it by the following procedure:

Procure a suspension of the organism to be tested by washing a 24-hour growth of this particular germ off an agar tube with an indefinite amount of normal salt solution. Shake the suspension well to avoid clumps. Collect some of the patient's blood from a finger-prick into a glass tube suitable for hanging in a centrifuge. By the same process procure blood from a healthy person to serve as a control. Centrifuge the blood in both tubes. Pipet off the serum from each tube and keep them separate. Pipet off some white blood corpuscles and wash them in normal salt solution. Now with a capillary pipet take equal volumes of the bacterial suspension, white corpuscles and the patient's blood serum and mix them. With another capillary pipet take equal volumes of the bacterial suspension, white corpuscles and serum from the control blood and mix them. The mixtures are now drawn into their respective pipets and incubated for fifteen minutes. Slides are then made from each pipet and stained with a suitable blood stain (Wright's or Hastings'). The germs found in from 30 to 50 leucocytes on each slide are counted and the total number of germs estimated on each slide are then added together and divided by the number of leucocytes counted. This will give the average number of germs ingested by the leucocytes suspended in the patient's serum, which figure is compared with that found by the same procedure using the control serum. In this manner one obtains the patient's opsonic index, or a comparative measure of the germ-destroying power of his blood.

GERM AND TISSUE FERMENTS.

During the past few years the enzyme or ferment theory of immunization, as worked out by Vaughan, Friedberger, Aberhalden and others is receiving most attention. This theory leads us to the most essential factor of life, digestion; and digestion depends on the presence of enzymes or ferments, because it is by means of these enzymes that

food substances are prepared, really dissolved, so they may be absorbed and assimilated. In the more highly developed forms of life the digestive organs are set aside for this purpose. Single cell organisms, on the other hand, are so constituted that all the functions of life are contained within the one cell. The single cell organism lives and grows by absorbing and assimilating food substances with which it comes in contact. Where necessary, the germ secretes enzymes from its surface for the purpose of digesting or dissolving this food so that it can be absorbed and assimilated, thereby carrying on its life function.

Of the various foods or substances that sustain life, protein occupies the most important position because tissue cells as well as single cell organisms are principally of protein composition. In fundamental construction, all proteins, whether of animal, vegetable or germ origin, are essentially the same; but animal as well as vegetable and germ proteins, obtained from various species, differ from one another in some specific character. The protein obtained from the blood serum of one species of animal will not circulate freely in the blood of an animal of some other species without producing serious physiologic disturbances. Horse serum protein when injected into a guinea-pig will produce certain definite physiological disturbances and the same is true when horse serum is injected into man. Eggwhite, and in fact all abnormal proteins, whether of animal, vegetable or germ origin, will produce the same disturbance under the same conditions. These disturbances were first observed as a result of animal experimentation in the production of antidiphtheritic serum and are now known as protein poisoning or anaphylaxis. An enormous amount of experimental research work has been done on this phenomenon of anaphylaxis and its relation to infectious diseases, and to comprehend the enzyme theory of immunization it is necessary to briefly bring forward its most important factors.

Of all animals, the guinea-pig has been found to give the most marked and most constant symptoms of protein poisoning, and for this reason is well adapted for studying this phenomenon.

Kolmer ("Infection, Immunity and Specific Therapy," 1915, p. 537) says: "Horse serum, when injected into normal guinea-pigs, gives rise to no symptoms. As much as 20 c.c. may be injected into the peritoneal cavity, and small amounts may even be injected into the brain, without causing any untoward symptoms."

"When a small dose of serum is injected intravenously, intraperitoneally, or subcutaneously, and ten days later a second injection is made, the animal develops symptoms of acute anaphylactic asphyxia, which, in the majority of instances, terminates fatally. In five or ten minutes after injection the pig becomes restless and then manifests indications of respiratory embarrassment by scratching at the mouth, coughing, and sometimes of spasmodic, rapid, or irregular breathing; the pig becomes agitated, and there is a discharge of urine and feces. This stage of exhilaration is soon followed by one of paresis or complete paralysis, with arrest of breathing. The pig is unable to stand, or, if it attempts to move, falls upon its side; when taken up it is limp; spasmodic, jerky and convulsive movements now supervene. This chain of symptoms is very characteristic, though they do not always follow in the order given. Pigs in the state of complete paralysis may fully recover, but usually convulsions appear and are almost invariably a forerunner of death. Symptoms appear about ten minutes after the injection has been given; occasionally in pigs not very susceptible they are delayed 30 to 45 minutes. Animals developing late symptoms are not very susceptible and do not die. Death usually occurs within an hour, and frequently in less than 30 minutes. If the second injection be made directly into the brain or circulation, the symptoms are manifested with explosive violence, the animal frequently dying within two or three minutes."—Rosenau.

The same symptoms would develop from inoculating guinea pigs with eggwhite or other animal or vegetable proteins in the same way, but no symptoms of anaphylaxis will develop unless the same kind of protein is employed in

the first and subsequent inoculations. Vaughan ("Protein Split Products in Relation to Immunity and Disease," chapter V) succeeded in splitting up various kinds of animal, vegetable and germ proteins by means of sodium hydroxide and absolute alcohol, and in this way obtained a substance constituting about one-third the original protein treated, which, when injected intravenously into guinea-pigs in 0.5 to 5 or more mg. doses, produces characteristic anaphylaxis with symptoms identical to those produced by serum inoculations.

Concerning the splitting of protein by ferments, Kolmer ("Infection, Immunity and Specific Therapy," 1915, p. 550) says:

"In 1910 Friedberger, by digesting a serum precipitate with normal guinea-pig serum, obtained a similar toxic substance; by means of ferments he secured a protein cleavage poison which, when injected into normal guinea-pigs, produced the symptoms of acute anaphylaxis, the process being entirely analogous to that obtained by Vaughan and Wheeler by protein splitting with alcoholic sodium hydroxid solution. Subsequent studies by Friedberger and his collaborators showed that similar protein poisons could be obtained by digesting microorganisms, as Bacillus prodigiosus, Bacillus typhosus, and Bacillus tuberculosis, with normal guinea-pig serum. Friedberger and Nathan obtained the poison by digesting normal horse serum with fresh guinea-pig serum; Bordet, by digesting agar with fresh serum; Dold and Aoki, by digesting meningococci, streptococci, pneumococci, gonococci, and various other microorganisms with fresh normal guinea-pig serum. As was expected, cleavage could be facilitated and hastened by using immune serum specific for any particular bacterial or other protein."

These experiments show that poisonous substance may be obtained from animal, vegetable or germ protein by disrupting the protein molecule with chemicals or by digesting it with blood serum. Normal blood serum contains a small amount of this digestive substance which has been called alexin, antibody, and by other names. This substance will digest a variety of proteins, more particularly

germ proteins, and constitutes the normal non-specific germicidal substance contained in the blood which is now regarded as a non-specific proteolytic ferment. When an abnormal protein gains entrance to the blood or tissues of the body which is not readily digested and disposed of by this non-specific proteolytic ferment, a protest in tissue cell activities develops with the production of a specific digestive substance which digests the abnormal protein. From our present knowledge this substance should be classed as a specific proteolytic ferment or enzyme specially prepared by tissue cells for this particular emergency. When this condition has developed the animal is said to be sensitized to that particular protein whether of animal, vegetable or germ origin. This sensitizing process starts to develop soon after the abnormal protein maintains its presence in the animal body, and in time is instrumental in developing a comparatively large amount of this specific proteolytic ferment. If a considerable amount of the same kind of protein to which an animal has been sensitized is injected after this ferment accumulation has taken place, sufficient specific proteolytic ferment is present in the body fluids to rapidly digest the injected protein and liberate so much of its toxic portion that poisonous symptoms develop. In other words, the animal has become highly immunized to that protein. Whatever the ultimate explanation of immunization may be, it is perfectly evident that protein sensitization with the development of specific proteolytic ferments by tissue cell activities does take place, and from this it is reasonable to assume that the various antibodies known as lysins, precipitins, agglutinins, opsonins, etc., represent different methods of ferment action.

The amount of serum necessary to sensitize a guinea-pig is surprisingly small. Rosenau and Anderson found one guinea-pig that was sensitized by 0.000,001 c.c. As a rule, they used less than 0.004 c.c. in their experiments.

Besredka places the minimum amount necessary to secure uniform results at 0.001 c.c., whereas 0.0001 c.c. proved sufficient in a considerable percentage of animals. The sensitizing dose of horse serum ordinarily employed in experiments upon guinea-pigs is 0.01 c.c.; amounts ranging from 0.001 c.c. to 1 c.c. are ordinarily followed by an incubation period of from ten to sixteen days. Large doses also sensitize, but a longer incubation period is required. In order to produce a fatal result a second or intoxicating dose must be considerably larger than the minimum sensitizing dose, the proportion between the two having been placed by Doerr and Russ as 1:1000; i. e., if 0.001 c.c. of serum is injected intraperitoneally in order to effect sensitization, 1 c.c. injected by the same route ten or twelve days later would in all probability kill a half-grown guinea-pig, whereas 0.1 c.c. subcutaneously would be followed by serious symptoms.

The knowledge obtained from studies of protein poisoning throws much light on the problem of infection and immunization. When an infection takes place, germs multiply in the tissues and fluids of the body, and, to the extent of their growth, a foreign protein is developed within the body. Here the non-specific proteolytic ferment, normally present in the fluids of the body, evidently was not sufficiently active as a foreign protein digestant, otherwise the infection could not have taken place; and, consequently, a reserve force of tissue cell activity is called out for the purpose of producing a specific proteolytic ferment which digests and destroys this foreign germ protein. In other words, the tissues are becoming sensitive to this particular germ protein. After sensitization has taken place, the protein molecule of the germ is disrupted, thus liberating its toxic radicle which gives symptoms of disease. In fact, Vaughan contends that all symptoms as a result of infection are principally due to this protein poisoning, and that the

main difference in the clinical manifestations of various diseases is due to the parts of the body or organs involved. This contention is receiving much support; but it is by no means generally accepted.

Others contend that germs, more particularly the staphylococci, streptococci, pneumococci, colon bacilli, typhoid bacilli, and similar organisms, contain endotoxins, and that symptoms of disease develop after the germs become disintegrated in the course of an infection and thus the endotoxin is liberated. Neither of these contentions would account for all the symptoms found in many rapidly progressing infections. Both the endotoxin and the split protein theory, as to the liberation of poisonous substances, assume that germ destruction is going on extensively where intense inflammatory and other toxic symptoms exist, while rapid germ development is also taking place at the same time. It is hard to reconcile these two factors. A cultural condition where germ destruction is progressing rapidly is never favorable for germ growth at the same time. Kolmer, in discussing the question regarding the source of poisonous symptoms, ("Infection, Immunity and Specific Therapy," p. 570) says: "Likewise in such infections as typhoid fever and pneumonia, I cannot eliminate the action of true toxins and endotoxins, and ascribe all the symptoms to the protein poison or anaphylatoxin. It is not always true that the incubation period is devoid of symptoms. Mild and evanescent symptoms are frequently present, and it is but natural to ascribe these to the effects of bacterial products themselves. After a time, when the bacteria have multiplied and reached special tissues, the symptoms become more intense and the typical lesions are produced. These may be ascribed to the result of the combined action of toxins themselves and the protein poison, rather than to the protein poison itself to the entire exclusion of the metabolic products of the bacteria. In the present state of our knowledge it is, of course, very difficult to decide which symptoms in a given disease are due to bacterial toxins, which to endotoxins, which to ptomains, which to mechanical action of the bacteria and which to the protein poison or anaphyla-

toxin. While it is perfectly true that we cannot understand symptoms as due to protein poison that cannot be ascribed entirely to toxins and endotoxins, it seems to me unwise to ascribe all lesions and symptoms to the toxins, on one hand, or the protein poison on the other."

The Digestive Ferments Produced by the Germs.

In speaking of toxins in this connection, I take it that Kolmer refers to substances which are produced by the germ, not a part of the germ structure.

Virulent infections, where germ multiplication and tissue disintegration are going on rapidly, show that activities by the live organism in maintaining its development and growth are important, if not the most important factors of such infections.

Vaughan ("Protein Split Products in Relation to Immunity and Disease," p. 208) in his experimental work found a pneumococcus so virulent that 0.000,001 c.c. of a 24-hour bouillon growth would kill a half-grown guinea-pig when injected intraperitoneally, while it required 1 c.c. of a regular stock culture to kill a pig similarly inoculated in the same length of time. In explaining the virulence of this organism he says: "Virulence may depend on several factors, but rate of multiplication is certainly one of them, and on a common medium as the animal body this must depend on the effectiveness of the ferments whose function it is to prepare and utilize the pabulum on which the organism feeds." Here special emphasis is placed on ferment secretion by the pneumococcus as a means of digesting its food for assimilation and that by efficient digestion and assimilation rapid growth and multiplication is made possible. Where such a pneumococcus infection is localized, this germ-produced ferment necessarily has a devitalizing or destructive influence on the involved tissue.

Simon ("Infection and Immunity," p. 33), in referring to difference in virulence of infecting organisms, says: "Two possibilities naturally suggest themselves, which may be operative either individually or conjointly. On the one

hand we may imagine that an organism, when introduced into the body of an animal which seeks to destroy the invader, adjusts itself to its new surroundings by certain changes of a morphological or physiological character, in consequence of which it becomes relatively or absolutely unassailable by the offensive forces of the host, unless, indeed, it already possesses such properties during its saprophytic existence outside of the body. On the other hand, we can conceive that the infecting organism actively secretes material which tends to counteract or even to destroy the opposing forces of the host."

Rosenow (Journal A. M. A., Sept. 7, 1912) demonstrated that pneumococci, during a process of autolysis in normal salt solution, produce a substance which has a very toxic influence, and when injected into animals, induces no immunizing responses but rather paralyzes the immunizing forces. He found that pleuritic effusion in cases of pneumonic empyema and pneumonic lung tissue also contain this toxic material. From this he concludes that during the process of toxic pneumonias a continuous autolyzing process of the pneumococcus takes place with the production of this toxic material which plays no part in bringing about an immunity but rather hinders antibody formation. I have good reason to believe that this toxic material is the result of ferment activities by the pneumococcus. A virulent streptococcus infection offers a good illustration:

Some years ago, before vaccine therapy came into use, I was called to treat one of these cases. This was a middle-aged woman of previous good health. While darning at 2 o'clock in the afternoon she pricked her thumb with the needle and soon after felt a distinct irritation associated with pain. Four hours later, when I was called to see her, she was suffering with severe pain in the thumb. The thumb was swollen, tender to the touch, and had a somewhat distinct cyanotic appearance. It was only by careful examination that the place where the needle entered could be found. The physical injury amounted to nothing, and I

could hardly imagine that so much inflammation could develop from infection by a needle-prick in so short a time, and concluded that a felon was developing and the needle-prick was merely co-incident. About 8 o'clock that same evening I was again asked to see the patient on account of severe pain in the thumb. I did not call, but prescribed some morphine. The next morning there was no longer any question about the needle-prick being the source of the trouble. There was a distinct area of intense inflammation with indications of necrotic tissue development where the needle had entered. A red lymphatic chain had developed which extended to the shoulder-joint. The lymphatic glands at the elbow were enlarged, and besides other symptoms of a virulent toxic infection there was a temperature of 102.5 degrees F. The condition was recognized as a case of streptococcus infection and this was later verified by bacterial examination. Here germ development was evidently going on very rapidly. Necessarily, the number of germs that were inoculated with the darning needle must have been comparatively small; but localized toxic symptoms developed soon after the inoculation. If it had been true that these poisonous substances which caused tissue irritation and inflammation were due to split proteins or endotoxins from destroyed germs, it is impossible that germ multiplication could have progressed so rapidly as the inflammatory extension indicated. To assist in overcoming this infection, 40 c.c. of antistreptococcus serum was given at once; but before the progress of the infection was overcome, a necrotic piece of tissue sloughed out where the needle had entered, extending almost to the bone and about three-eighths of an inch in diameter. The most logical explanation concerning the rapid germ development in this case is that the germs produced some substance that had a destructive or devitalizing influence upon the tissues in the infected area which aided the germs in their growth and multiplication, but did not have any material influence in stimulating cell activities toward producing immunizing

substances. Every practicing physician has seen these cases of severe infection, and where immunotherapy has not been applied he has almost invariably seen them run a long course and sometimes have a fatal termination.

It is reasonable to assume that germs have no intent or purpose in their development. They simply grow and multiply to perpetuate themselves. When they gain entrance to the tissues of the animal body, they must utilize substances with which they come in contact for nourishment and if such substances are not available they must die. For the germ to remain alive, digestion, so its food can be assimilated, is necessary. This digestion is accomplished by the action of ferments. When the food is not suitable for absorption, the germ secretes a ferment which digests the food substance with which it comes in contact. This enables the germ to multiply rapidly because this ferment cripples or destroys the defensive forces of the tissue cells with which it comes in contact. From the way infections progress under the influence of these germ produced ferments, we have a right to assume that these ferments do not actively influence cell activities in the direction of specific proteolytic ferment production for the destruction of the invading organism but, on the contrary, hinder the production of immunzing substances. If these toxic, germ-produced ferments were active stimulants for antibody production, infective processes would be self-limited because the time would inevitably be reached in every acute infective process where the immunizing apparatus would be sufficiently stimulated to bring about an immunity; but in active practice we often find the reverse to be the case. Instead of the patient becoming immune to the infecting organism, he dies, not from tissue exhaustion, but from toxemia or paralysis of the nerve centers.

IMMUNITY.

Immunity may be natural or acquired. Natural immunity may be explained on the theory that the non-specific proteolytic ferments contained in the blood serum

of one species will digest and destroy germs that may be able to live and cause disease in some other species. Acquired immunity may be active or passive. An active immunity may be obtained by the tissue cells becoming sensitized for the production of specific proteolytic ferments as a result of an infection or from germ inoculations. A passive immunity may be brought about by injecting or supplying immune serum obtained from some immunized animal, as is being so successfully done in the treatment of diphtheria or tetanus with antidiphtheritic and antitetanic serum. In this instance, the animal from which the serum was procured produced the antibody; whereas in an active immunity the tissue cells of the person becoming immunized produce the antibody.

INFECTIONS AS IMMUNO-PRODUCERS.

The severity of an infection depends upon the virulence of an infecting organism and the resistance the host may have to a given germ invasion. A very virulent organism may cause but slight disturbance in some individuals while a much less virulent organism may cause a very severe infection in someone else. Furthermore, the condition known as "being in excellent health" is no guarantee that virulent infections may not take place; nor does it follow that one in ill health is necessarily very susceptible to infection. It is a common experience to see vigorous, healthy individuals come down with typhoid fever and die, while the less robust may have a mild attack or escape infection entirely. The same may be said of pneumonia, scarlet fever, diphtheria, infected wounds, and many other ailments. The all-important factor in resisting germ invasions consists in developing proteolytic sensitization, which constitutes the establishment of an immunity towards the various organisms causing infectious diseases.

In some diseases, one attack will develop a proteolytic sensitization of such intensity that the immunity will con-

tinue through life. Of these measles, small-pox, chicken-pox, whooping cough, scarlet fever, typhoid and yellow fever are good examples. In other diseases, especially those produced by the more common pathogenic organisms, staphylococci, streptococci, pneumococci, colon bacilli, etc., immunities sufficient to overcome a given infection will soon wear off, making subsequent attacks possible.

Recovery from a virulent infecting organism does not insure a greater measure or a more intense degree of immunity than recovery from an infection caused by a much less virulent organism of the same variety. A person who has recovered from a severe attack of typhoid fever, small-pox, or scarlet fever during an epidemic of these diseases in which highly virulent organisms are prevalent does not possess a more intense immunity than one who has recovered from the same disease during an epidemic in which less virulent organisms were prevalent. In fact, an infection by a virulent organism will overwhelm or break down the immunizing mechanism in the more susceptible and result in death; whereas an attack by a markedly less virulent organism will result in the establishment of an immunity sufficient to overcome the existing infection, and the immunity thus established is also efficient in preventing later infections in this class of infections by even more virulent types of organisms.

IMMUNITY PRODUCED BY INOCULATING ATTENUATED ORGANISMS.

This fundamental principle is taken advantage of in prophylactic inoculations against small-pox. Here a non-virulent organism closely related to the small-pox germ is inoculated, and the immunity which is established in getting rid of this non-virulent organism, also protects against infections by virulent small-pox germs.

Pasteur accidently discovered that chicken cholera germs that had been cultivated under unfavorable conditions, no longer produced ill effects when inoculated into healthy chickens, but at the same time immunized the

chicken against the virulent organism. This discovery laid the foundation for proteolytic immunization by attenuated organisms which is now being successfully employed in man. Kolmer, (Infection, Immunity and Specific Therapy, 1915, p. 611), says: "An active immunity may be acquired by inoculation with antigen so modified or attenuated that it can stimulate the production of specific antibodies without producing the disease or otherwise greatly disturbing the health of the individual."

With most pathogenic organisms there is more or less danger in inoculating attenuated live organisms, because of the possibility that they might revert back in particularly susceptible individuals and become pathogenic agents. For this reason, killed organisms are usually employed for prophylactic inoculations; and, experience shows that just as good immunizing responses may be obtained—if the organisms are killed without applying too much heat or unsuitable chemicals—by repeated inoculations at proper intervals, as if attenuated live organisms had been employed. This has been most conclusively demonstrated in recent years by prophylactic work. There is no more striking illustration as to what can be accomplished in this direction than the results secured from the use of typhoid vaccine in the prevention of typhoid fever in the American and European armies, in the protection of nurses in hospitals, in insane asylums and other public institutions, and among communities in the presence of typhoid epidemics. The same may be said of the use of meningococcus vaccine in the prevention of cerebro-spinal meningitis, as shown by the reports of the health department of Texas during the meningococcus epidemic in that state which occured in the winter of 1912-1913.

The value of whooping cough vaccine in the prevention of whooping cough is now also well established. Preventive inoculations are, further, being successfully employed

in cholera and plague, and the same principle is steadily being applied toward preventing other infectious diseases, as the typhus vaccine of Plotz in Serbia.

The value of vaccine inoculation for the prevention of disease is so easily recognized that there is no longer room for doubt. It is easy of demonstration and the fundamental principles involved do not come in conflict with well established conceptions. It is different, however, when we consider the advisability of giving a vaccine in the presence of an infection. Here the question naturally arises: If the live organisms causing the infection do not arouse sufficient tissue cell activities for the production of immunizing substances, why should vaccine inoculations hasten such activities? In considering this question, certain basic facts that we have learned from prophylactic inoculations must be taken into consideration. That recovery from a virulent infection does not establish a greater measure or a more lasting immunity than a recovery from a much less virulent type of the same organism, shows that antibody formation does not depend on the degree of virulence possessed by the infecting germ. Attenuated organisms, germs that have in a measure been crippled in their activities by unfavorable surroundings or cultural conditions, may have been so modified that when injected into susceptible animals they will not cause any material disturbance and yet cause the development of sufficient immunizing resistance so that the animal is no longer susceptible to an attack of the virulent type. This clearly demonstrates that living cell activities respond to attenuated organisms more readily than to virulent germs with the production of specific proteolytic ferments or immunizing substances.

In the application of rabies vaccine to one bitten by a mad dog, we are directly involved in this problem of active therapeutic immunization with attenuated organisms.

Here we have an infection of a virulent organism. The infection is evidently active because it is only a question of time when the victim will show symptoms of disease and probably die. Rabies vaccine consists of rabies organisms so attenuated that they are no longer capable of producing harmful symptoms in man. When these attenuated rabies organisms, being abnormal intruders, are injected under the skin, cell activities take place to get rid of them. Now, the essential difference between the attenuated inoculated rabies organisms and the virulent rabies germs inoculated by the dog bite, so far as their relation to tissue cell activities in their destruction is concerned, is that the virulent germs offer a greater resistance to destruction by the living cells of the host than the attenuated, crippled organisms do, that were contained in the inoculated vaccine; and it is in the capacity of cell activity to destroy these germs that specific enzyme production, sensitization, immunization takes place. In other words, the less virulent organisms are more readily attacked by tissue cells than the virulent ones, and consequently, antibodies for their destruction are proportionately more readily produced. In compliance with the physiologic law that immunities which have become established, as a result of tissue cell activities, in disposing or eliminating non-virulent organisms, will also be efficient in eliminating or destroying virulent organisms; the immunity established from the rabies vaccine inoculation also destroys the virulent organisms inoculated by the dog bite, and in this way eliminates the danger of the rabies infection.

All this clearly indicates that, during active infections, forces are at work which hinder specific proteolytic ferment production and that this hindrance is linked with the activities of a living organism in its attempt to maintain itself by feeding upon the available substances probably through ferment secretion; that, for this reason, virulent, live organisms are not suited as antigens in stimulating

tissue cells for rapid antibody formation; and, that attenuated or killed organisms, in so far as they do not resist tissue cell activities, are more suitable for rapid sensitization in specific proteolytic ferment production. It is this principle that is taken advantage of in applying vaccines in combating infections.

THERAPEUTIC IMMUNIZATION WITH KILLED ORGANISMS.

When we come to applying bacterial vaccines to the treatment of active infections, this principle of hastening immunization by injecting attenuated organisms, organisms that tissue cells can readily dispose of, is carried one step forward, that of killing the organisms used for this purpose. And this step has carried us to an epoch-making period in the treatment of disease to a therapeutic measure by means of which active immunization may be hastened during the course of an infection. While it is true that Pasteur, Koch, and others treated infections with bacterial products before Wright, yet it was his work that placed vaccine therapy on a firm practical basis. His system of standardizing killed bacterial suspensions, by determining the number of organisms per cubic centimeter, made accurate dosage possible. By means of his opsonic index he was enabled to follow at least one angle of the immunizing process and thereby definitely determine whether a given dose of vaccine stimulated an immunizing response or, possibly, produced a depressing effect. He soon demonstrated that surprisingly small doses were sufficient to immunize, whereas large doses did not result so favorably. This is in accord with experimental research work on protein sensitization. Rosenau and Anderson succeeded in sensitizing a guinea-pig with 0.000,001 c. c. of horse serum. This would equal about 0.00008 mg. of horse serum protein. It is found that 0.001 c. c. of horse serum will sensitize guinea-pigs more regularly, and in less time than larger doses. Wright found that doses ranging from five million

to several hundred million or one billion organisms, varying with different varieties of germs, was sufficient to stimulate immunizing responses. These figures are large and to the casual observer they might appear to be enormous doses; but germs are exceedingly small and this can only be thoroughly appreciated when the weight of millions of these organisms is reduced to the fraction of milligram or grain. According to Wilson and Dickson (Journal of Hygiene, May 3, 1912, No. 1, Vol. XII, p. 56), 50,000,000 streptococci, an average dose, would weigh approximately 0.015 mg. or 0.000231 grain.

When we consider the advisability of injecting killed bacterial suspensions in a case of extensive active infection with fever and other symptoms of severe toxic disturbances the question naturally arises: Why should inoculations of killed organisms hasten active immunization where toxic conditions, as a result of the infection, already exist? Why add more toxic material in the form of a vaccine to a system loaded with toxic materials? Here the infection is not in the incubation stage as in the case of rabies infection and, furthermore, where rabies vaccine is given after symptoms of disease have once developed, it is no longer of value.

In considering this question it is necessary to realize that the presence of extensive toxic symptoms in an acute infection is no evidence that the immunizing mechanism is being actively stimulated. On the contrary, this would show that immunization is being retarded, evidently due to devitalizing influences as a result of live organism activities. All our experience in prophylactic immunization shows that devitalized or killed organisms are better immuno-producers than virulent live germs, and experience also shows that this immuno-producing influence of killed organism inoculations will take place during the course of an infection as effectively as when used for prophylactic purposes.

Let us take a case of streptococcus infection like the one previously referred to. Here we have a virulent infection that is progressing rapidly from a slight injury. Specific sensitization for germ-destroying antibody production is evidently retarded, because germ multiplication is going on rapidly as shown by extensions of the infected area. During the early stages of such an infection much healthy tissue remains which may be utilized for antibody production. By injecting into this healthy tissue a suitable number of killed germs of the same kind that are present in the infected area, being intruders which have the essential biochemical constituents possessed by infecting organisms, these tissue cells become active in disposing of or destroying them. Not being aware that the inoculated germs are killed, the same efforts are put forward as if an active focus of infection had taken place. The germs being killed, they can offer no resistance to cell activities nor can they secrete digestive ferments that have a devitalizing influence on the tissue cells with which they come in contact and, consequently, the entire cell energy may be directed toward producing specific proteolytic ferments.

When cells have once become sensitized for specific ferment production, they continue to produce such ferment for some time after the organisms which caused this sensitization are disposed of. This proteolytic ferment or antibody is then conveyed, by means of the circulating blood, to the infected area and there aids the involved tissues in overcoming the infecting organisms according to the principle that antibodies which have been formed for the destruction of attenuated or devitalized organisms are equally efficient in destroying virulent organisms of the same variety with results that often look magical.

Naturally, the earlier in the course of the infection the vaccine is applied the better the result. I have repeatedly seen active, virulent streptococcus infections aborted with

the timely application of streptococcus vaccine. It is a common experience to see such cases become quiescent in one or two days with a drop in temperature from 102 or 103 to normal after one or two inoculations and go on to rapid recovery, if the infection has not been allowed to become too extensive before the vaccine was employed.

The use of vaccines in the treatment of furunculosis offers a good illustration that killed organisms, when injected under the skin, are better immuno-producing antigens than the live organisms causing the furuncles. In some of these cases repeated crops of furuncles appear, keeping the patient in misery for months, in which every furuncle will produce more local and constitutional disturbance than a single dose of staphylococcus vaccine; and yet the one dose of vaccine will develop more immunity than resulted from the combined influence of all the previous furuncles. Small furuncles that have started to develop will dry up, while the indurated area around those further advanced will soften, leaving a small abscess near the surface which will, on being opened, heal rapidly; and after a few more inoculations at four or five-day intervals, the entire trouble becomes eliminated. This the immunizing mechanism was not able to accomplish under the influence of live organisms during months and possibly years of activity. In fact, infections by some organisms appear to have a tendency to break down immunizing resistance, whereas repeated inoculations of killed organisms of the same variety have a tendency to build up an immunity. It is a common experience to find that where a staphylococcus carbuncle developes several more similar carbuncles may be soon looked for. Recovery from an attack of pneumonia does not establish a permanent immunity, but seems to make the subject more liable to future attack. The same may be said of erysipelas. Some people are particularly susceptible to taking "colds" or to tonsillar infections which

are usually due to pneumococcus or streptococcus activities. Spontaneous recovery from rheumatic fever makes the subject particularly susceptible to future attacks which may finally develope into chronic arthritis. When these cases are treated by the application of immuno-therapy with injections of killed bacterial suspensions, these relapses occur comparatively seldom, and especially so if vaccine inoculations are made for a reasonable length of time after recovery has taken place. The only way we can account for this is that a more complete and intense sensitization for specific proteolytic ferment production is developed under the influence of repeated injections of killed organisms than from active infections by live organisms.

Many theoretical objections have been advanced against the use of bacterial vaccines in acute general infections, cases where the germs have invaded the circulating blood, on the contention that these invading organisms furnish sufficient stimulus to tissue cells for a maximum antibody production. It must be admitted that at first thought it does not look reasonable to expect any benefit from injecting killed organisms where the entire system is invaded with live germs, but on closer investigation it is found that conditions prevail which are not apparent at first.

It is well known that normal blood serum contains bactericidal substances for a large variety of pathogenic bacteria; that if a certain organism gains entrance to the blood stream and maintains itself there it is evident that germ-destroying substances for this particular organism are not adequate for the occasion. Evidently the live organism offers a certain resistance to destruction, and until active destruction of the germ takes place no sensitization for specific antibody formation has taken place. It is remarkable how the tissue structures of the various parts of the body avoid the infecting organisms and prevent localization, when we consider the enormous number of organisms which

are present in the circulating blood in these cases. And when localization does take place, certain kinds of organisms have a distinct tendency to invade certain organs, while others may localize in almost any part of the body. Thus the pneumococcus attacks the lung tissue, certain streptococci the heart or joint structures, the meningococcus the cerebral and spinal meninges, etc., while staphylococci have no special predilection for localization while circulating in the blood; but active antibody formation for the eradication of the infecting organism from the blood does not take place until localization of the infection has taken place. In this connection Allen ("Vaccine Therapy and Opsonic Therapy," Fourth Edition, p. 267) says: "Antibodies are not formed in the general circulation, but in the blood-forming organs, muscles, and subcutaneous tissues. It therefore follows that it is only when circulating bacteria have been trapped in such localities that any stimulus is given to the formation of antibodies." By injecting killed bacterial suspensions in such cases we have the distinct advantage of obtaining localization of tissue cell activities for antibody production and this is accomplished with an antigen that offers no resistance so a full measure of antibody may be produced.

The unquestionable practical results that have been obtained in the treatment of blood invasions by streptococci, pneumococci, staphylococci, gonococci, typhoid bacilli, and other organisms by vaccine inoculations, when used reasonably early, justifies this conception as to the workings of the immunizing mechanism under the influence of killed germ inoculations, in acute general infections.

The objection that bacterial vaccine injections are not practical in acute infections on the ground that it requires four or more days for antibody formation to take place from such inoculations and that, meantime, a sufficient antigenic stimulus will have developed by the infecting organisms to

cause a maximum antibody formation, is not sustained by experience. The simple fact that it requires considerable time to develop a measurable amount of precipitins, agglutinins, lysins, etc., from vaccine inoculations in healthy individuals is no evidence that antibody formation has not had an earlier existence; furthermore, there is good reason to believe that tissue cells act more promptly to vaccine inoculations in the presence of an infection than otherwise. Opsonic index determinations usually show increased opsonic production within 24 hours after a vaccine inoculation in the presence of acute infections. Besides this, clinical evidence shows that marked improvement usually takes place within one to three days. In this connection Allen, of London, says: "The attempt, therefore, to induce on the second or third day an artificial crisis in pneumonia, which normally would not occur until the seventh or eighth, or an immediate defervescence in typhoid fever which would otherwise be delayed for many days, may therefore be justified, and practical experience, so far as it goes, does not contra-indicate the procedure." In the early days of acute infections, tissue cells are not exhausted in their defensive powers and a dose of vaccine is so small that its toxic content, for all practical purposes, amounts to nothing as compared to the toxic substances that are continually being evolved from the existing infection, while at the same time the vaccine contains enough devitalized organisms to stimulate specific antibody production for the destruction of the infecting organisms.

There is good reason to believe that there are various degrees or stages of disintegration in the disposition of bacteria and bacterial products by these proteolytic ferments or enzymes, and that when the disintegration is incomplete, toxic or poisonous symptoms develop. Greely (Journal A. M. A., Feb. 6, 1915), in considering the problem, says:

"Any individual becomes what is called sensitized to an infecting organism soon after it or its products gain access to the general circulation, and as this means that his lymph contains newly developed enzymes peculiarly adapted to the disintegration of the special bacterial protoplasm involved, no sooner does such protoplasm find its way into his tissues than it is attacked and more or less completely digested. The symptoms arising from this process depend directly on the activity and quantity of such enzymes that may be available, no less than on the quantity of bacterial matter introduced. If these two factors are so related that immediate and complete disintegration of the bacterial matter takes place, no symptoms whatever occur. But if the digestive process proceeds relatively slowly, as with our gastro-enteric digestion of albumin, through albumose and peptone to amino-acids, the poisonous action of the intermediate products shows itself in symptoms of inflammation at the point of introduction * * *; in fever, increased pulse rate and malaise generally."

The prompt relief from fever and other toxic symptoms, often within 18 to 24 hours after vaccine inoculations, when used early in severe acute infections like pneumonia, puerperal sepsis, erysipelas, typhoid fever, and so forth, indicates that vaccine inoculations hasten antibody production to such a high degree of efficiency that toxic materials are largely or entirely disposed of.

Bacterial Vaccines in Chronic Infections.

Chronic infections present a condition in which the living cells of the host have developed a certain tolerance to the presence of micro-organisms. This is evidently due to a certain resistance that the invading organism offers to destruction by antibody formation, specific proteolytic sensitization not having developed to a point of sufficient intensity to eradicate the infection. Here vaccine inoculations are clearly indicated, at least in such diseases as come under the domain of vaccine therapy. In the application of vaccine therapy in chronic infections we find

that results are good, as a rule, yet they are not so striking and decisive as when applied in the early stages of acute infections. This may be accounted for on the ground that in chronic infections repeated auto-inoculations have, in a measure, exhausted or crippled the immunizing mechanism, or that extensive inflammatory deposits hinder a free supply of immunized blood to gain access to the infected area.

The underlying principle involved in the action of vaccines in chronic infections is the same as in the acute varieties. In the treatment of chronic infections, however, we find that reactions are more pronounced, both local, at the point of inoculation, and general; that, as a rule, smaller doses should be applied than in severe acute cases, and that inoculations should be made at somewhat longer intervals. Why this condition prevails I will not attempt to explain here. Most reaction is usually observed after the first inoculation, subsequent inoculations producing less reaction under increasing dosage. Since vaccine inoculations are particularly efficient in acute infections, I am persuaded that if they were regularly used in the treatment of acute diseases, chronic ailments due to infections would be avoided.

VACCINES ARE NOT SERUMS.

For some reason there is still considerable confusion in the minds of many physicians as to the difference between bacterial vaccines and therapeutic serums; in fact, they seem to think that they are essentially the same. Unless a physician understands the essential difference between these two therapeutic measures, he can apply neither to the best advantage. This confusion has in all probability arisen because both remedies are applied as immunizing agents, the difference between active and passive immunization not being sufficiently recognized.

From the foregoing it is clear that bacterial vaccines are suspensions of killed germs and when injected hasten the establishment of an active immunity by stimulating tissue cells for the production of antibodies; whereas, a therapeutic serum consists of blood serum obtained from a lower animal which has been immunized by repeated injections of germs or germ products until a high degree of immunity has been obtained, and by injecting this serum, antibody that has been prepared by immunizing the animal is supplied to the patient to aid in overcoming the infection. This is passive immunization; because the cells of the host have not been active in bringing it about. This kind of an immunity is not as permanent as an active immunity because the immunizing substances which have been injected with the foreign serum will soon be eliminated. Furthermore, antibodies obtained from immunized animals are always tied up with a large amount of foreign protein contained in the blood serum and by repeated injections of therapeutic serums, protein sensitization, anaphylaxis, or serum sickness is likely to develop.

As has been pointed out, the protein content of a dose of bacterial vaccine is very small and a surprisingly small amount of foreign protein will produce specific proteolytic sensitization. An average dose of a bacterial vaccine ranges from 0.05 to 0.1 mg., whereas 10 c.c., an average dose of therapeutic serum, contains 800 mg. of protein, a sufficient amount to cause protein poisoning or anaphylaxis on repeating inoculations. In applying bacterial vaccines and immune sera as therapeutic agents, these two facts must be kept in mind: Bacterial vaccines are always given in very small sensitizing doses, and for that reason they may be repeated indefinitely, the dose never being large enough to cause poisonous anaphylactic reactions; therapeutic serums contain a large amount of protein, making repeated inoculations hazardous because the resulting protein sensi-

tization may cause a dangerous anaphylaxis from reinjections of the serum.

The fact that large doses of protein are given when immune sera are employed is not sufficiently appreciated. I have frequently seen objection to using mixed vaccine on the ground that the additional organisms in the vaccine to which no corresponding infection exists would unnecessarily hinder the immunizing mechanism, while immune sera are recommended at the same time because ready prepared immune substances are by this means given to the patient; but, that thousands of times more abnormal protein is given than is present in a mixed vaccine which must be disposed of through cell sensitization and necessarily causes marked disturbances, is here not considered. This was forcibly impressed on my mind a few years ago in a conversation with a prominent surgeon in Cincinnati. He was treating a case of sepsis with purulent peritonitis. The peritoneal cavity was being drained and a large amount of antistreptococcus serum had been given in 40 c.c. doses. He pointed out that the patient had a very erratic temperature, ranging from subnormal to 106; the temperature sometimes fluctuating several times during the day. I suggested that probably a large part of that temperature was due to protein sensitization from the antistreptococcus serum that had been given. On my suggestion the serum was discontinued and a mixed vaccine given, with a resulting recovery.

CHAPTER II.

ARE VACCINES DANGEROUS?

In the development of vaccine therapy many theoretical criticisms have been advanced and alleged dangers have been pointed out by its opponents, who have ignored the actual experience of extensive vaccine users in the clinical field. Curiously enough, the most strenuous critics of the general application of bacterial vaccines have had little or no experience which would justify any opinion at all. Many such criticisms have been brought forward even by men of high repute in the science of immunology, and no doubt the wide publicity that these theoretical objections received has been responsible for non-resort to vaccine therapy in many cases in which vaccines should have been applied—to my mind, with an unquestionable loss of many lives that could have been saved and the prolonging of much suffering that could have been avoided. Theoretical objections have no place, when they conflict with the teachings of experience. When diphtheria antitoxin was first introduced, many diphtheria patients were allowed to die, who might have been saved by the timely application of this wonderful discovery, because some skeptics considered it a dangerous remedy. My experience with the use of bacterial vaccines has certainly been sufficiently extensive to bring out the dangers from their therapeutic or prophylactic application, if there were any. I have myself administered many thousands of doses and have given them in extremely acute, in subacute, and in chronic cases; to young infants, to adults, and to the aged, without ever seeing any dangerous reactions; nor have I ever heard any complaint of dangerous results following vaccine inoculations from the many physicians whose use of vaccines would total many million doses.

The theoretical dangers of vaccine injections are: 1. Protein poisoning or anaphylaxis. 2. The negative phase. 3. Adding toxic material to a system already overloaded with toxins.

PROTEIN POISONING.

Occasional dangerous anaphylactic reactions from the use of therapeutic serums has led some doctors to think that because germs are chiefly composed of protein, killed germ inoculations in the form of a bacterin would also be liable to produce anaphylaxis.

Vaughan ("Protein Split Products in Relation to Immunity and Disease," p. 236) points out that all proteins contain a poisonous group and that this poison is sufficiently violent to kill a guinea-pig in doses of 0.5 mg. when injected intravenously. According to Vaughan this poisonous protein constitutes about one-third of the entire protein substance. From this it would follow that it would require 1.5 mg. of protein to kill a guinea-pig sensitized to that particular protein. Besredka found by actual experiment that the smallest killing dose for a sensitized guinea-pig is about 2 mg. of protein. The comparative weight of man to a guinea-pig is about 1 to 300. This would make the minimum killing dose of a protein to which an individual is sensitized not less than 450 mg. The amount of protein contained in an average dose of mixed vaccine weighs less than 1/10 mg. Using these figures as a basis the calculation is simple: If 450 mg. of protein is a minimum fatal dose for a sensitized man it would require 10 x 450 mg., or 4,500 times the average dose of a vaccine to produce a fatal protein poisoning. The average initial dose of vaccine is 0.5 c.c. On this basis it would require two quarts of an average bacterial vaccine to contain enough protein poison for a fatal dose.

Vaughan ("Protein Split Products in Relation to Immunity and Disease," p. 122) finds that it requires doses of about 1 to 40,000 of body weight of killed dry colon bacilli injected intraperitoneally to invariably kill a guinea-pig inside of twelve hours. According to this, it would require 6.25 mg. of dead dry colon bacilli to kill a 250 grm. pig and if man is no more susceptible to colon bacilli it would proportionately require 300 times 6.25 mg. of the dried organisms or 1,875 mg. to invariably kill a man. We seldom give more than 320,000,000 colon bacilli as an initial therapeutic dose. This would amount to 1/20 mg. of dried colon bacilli. In other words, a dose of 320,000,000 or 1/20 mg. of killed colon bacilli is sufficient to sensitize or arouse an immunizing response, but it would require 37,500 times this amount —sufficient colon bacilli to make five gallons of an average colon vaccine—to invariably kill a man weighing 150 pounds. The application of typhoid vaccine for prophylactic purposes is one of the most conclusive demonstrations that it requires but a small amount of a bacterial suspension to develop a sensitizing or immunizing response. The usual initial dose is about 500,000,000 organisms or about 1/16 mg. of dried typhoid bacilli.

These calculations most conclusively show that there is not enough protein in the average dose of mixed vaccine to produce protein poisoning. It may be contended that it is not the small amount of protein contained in the vaccine that is the source of danger, but that the giving of a dose of vaccine, where an extensive infection exists, might sensitize the patient so rapidly that the poisonous materials set free from the resulting rapid disintegration of the numerous germs constituting the infection would overwhelm the patient and cause death. Such a contention can only be verified by actual experience. Fortunately, bacterial vaccines have been extensively employed for a sufficient length of time to definitely settle this question.

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Typhoid vaccine has been extensively employed in the treatment of typhoid fever and so far not a single case has been reported where symptoms of protein poisoning followed its use. On the contrary, all extensive users of typhoid vaccine in the treatment of typhoid are agreed that the nervous system, particularly, is materially benefited by this treatment, the mind remaining clear and the patient appearing brighter, not so restless, feeling stronger and less evidence of suffering. The temperature runs a modified course, especially so if treatment is started early in the course of the disease. No marked rise of temperature or other symptoms of intoxication follow the vaccine injection and this applies in the extremely advanced cases as well as in the milder forms. Mixed vaccines have been extensively employed in lobar pneumonia and puerperal sepsis in every stage of the disease without the least indication of toxic reactions following their administration. On the contrary, it is found that in these extremely acute infections, the patients tolerate large doses better, have less inflammatory reactions at the point of inoculation and show less tendency to a slight rise in temperature due to the vaccine than in subacute and chronic infections. Furthermore, inoculations may also be made at much shorter intervals—once or twice daily—to advantage, whereas in chronic cases vaccines are given at from four to seven days apart. The temperature drops materially within 24 hours after the first inoculation with proportionate other clinical improvements, especially so if the vaccine is given early in the course of the disease.

Guinea-pig inoculations have been repeatedly resorted to with large doses of bacterial vaccines without producing bad effects. I gave one guinea-pig subcutaneously a dose of mixed vaccine containing Friedlander bacillus 5,400,000,000, micrococcus catarrhalis 3,600,000,000, pneumococcus 1,440,000,000, streptococcus 1,080,000,000, staphylococcus albus 3,600,000,000, and staphylococcus aureus

3,600,000,000, without ill effect; a moderate inflammatory area at the point of inoculation was all that could be noticed. This number of organisms is equivalent to the content of a bulk package containing 18 c.c. of vaccine regularly in use, and would represent a dose equivalent to 8,000 times the amount given for therapeutic purposes in man.

The contention that doctors are not inclined to publish their failures when employing new remedies is no doubt true, but if harmful results were observed the maker of the product would no doubt hear from them at once. I find that even such a trivial affair as a small abscess development at the point of vaccine inoculation, which may be due to a peculiar susceptibility of the patient or to some carelessness of the doctor himself, brings forth urgent inquiries at once; naturally a much more vigorous inquiry would put in its appearance if something really dangerous happened after a vaccine inoculation. Certainly no such inquiry ever reached me.

THE NEGATIVE PHASE.

The possibility of a negative phase as a dangerous factor in giving vaccines is no longer receiving the serious consideration that it formerly did, experience having demonstrated that this phenomenon does not extend over a sufficient period of time to be of clinical importance in infections by the usual micro-organisms, and especially not in the early stages of severe acute infections. Wright was impressed with the operations of the negative phase because opsonic readings demonstrated that, for a variable length of time after vaccine inoculations, a diminished amount of opsonin was found in the blood which later on was followed by a marked increase of opsonin. From this he concluded that infecting organisms might become particularly active during an infection or during the stage of

incubation, if this negative phase should follow a vaccine inoculation, but opsonin formation is only one angle of the immunizing process, other antibodies also being formed. It was thought that on account of the negative phase, typhoid fever vaccine inoculations for prophylactic purposes, if employed during the incubative stage, might be a dangerous procedure. In this connection Russell says that he has seen no evidence of a negative phase from typhoid vaccine inoculations under any condition. What is true of typhoid infections concerning the negative phase applies equally to most other micro-organisms. A notable exception to this quite general action of vaccine, however, is the action of tuberculin (either O. T., T. B. or B. E.), which is quite toxic in cases of tuberculosis, where it must be given very cautiously and in extremely small doses at comparatively long intervals to avoid a negative phase.

ADDING TOXIC MATERIAL TO A TOXIC SYSTEM.

The question of possible danger from adding toxic material to a patient that is already loaded with toxic substances from an extensive infection is best met by pointing out that a dose of vaccine is entirely too small to have any material influence in producing toxic symptoms in addition to those already present. In an extremely toxic infection more germs will probably develop during every hour of the day than the number of the killed germs inoculated amounts to. Furthermore, the germs thus evolved are living organisms which have a tendency to multiply and retard immunization, whereas the killed germs inoculated into healthy tissue have a distinct immunizing tendency.

This question of possible dangers in using vaccines has been quite extensively considered in medical literature and I think a few abstracts and quotations on this subject will be of interest.

Simon ("Infection and Immunity," p. 198) says: "While acute infections have generally been regarded as contra-indicating the use of vaccines, this has largely been on theoretical grounds. Personally, I have gained the impression that vaccination, even in such cases, could do some good."

From an editorial (Amer. Jour. Physiol. Therap., 1910, 1, P. 190) I quote the following:

"The growth of vaccine therapy—that most wonderful addition to the possibilities of the work of the general practitioner—has been hampered to a considerable extent by a mistaken and exaggerated fear of the dangers of the so-called 'negative phase.'

"Vaccines are not dangerous. This statement is made with all due deference to the feelings of many whose articles and statements we have read and heard. We qualify our statement by adding 'if properly used.' It is evident that the utilization of bacterial vaccines carries with it possibilities of harm; but no more so than the use of every drug in the Materia Medica and, for that matter, every procedure in physiologic therapeutics.

"In our opinion the majority of the profession, by more widely adopting vaccine therapy, would be doing themselves a benefit which would increase their control over many of the germ diseases (particularly those of a chronic nature) and incidentally add in a large measure to their professional prestige—and their remuneration."

As a convincing object-lesson I also quote here several interesting paragraphs from an article on this subject by Professor Timothy Leary, of Boston:

"These objections to the use of vaccines in infectious conditions seem to focus themselves against their use in general infections. They will therefore be considered here. The general harmlessness of vaccines is indicated by two cases of infection in which, through error, 10 c.c. of staphylococcus pyogenes aureus vaccine containing 10,000,000,000 organisms were injected at one time as an initial dose. In one case no untoward symptoms appeared. In the second there was a temporary collapse with prompt response to heat and stimulation. There are few powerful drugs in the pharmacopeia which could be used with such disregard for dosage without serious results.

"The most serious objection to the use of vaccines in general infections is that the patient is undergoing extreme intoxication. I have called attention to our theory of muscle immunity, and to the fact that physiological doses of vaccines are not followed by a toxic (negative) phase. The dose of vaccine used in pneumonia, for example, contains fewer organisms than will be found in a few out of the myriads of infected air sacs of the lung in this disease. The dosage is so infinitesimal, and its toxic effect is so slight, if any, that it is not measurable. As evidence that even much larger doses are at least harmless, I might cite the case of a child 7 years undergoing an infection with pneumonia, with a temperature of 103 degrees and extreme meningeal symptoms, into whose body was injected, as an initial dose, 1,600,000,000 pneumococci. The standard dose for adults is 8 minims, or 100,000,000 pneumococci. This child, receiving sixteen times the adult dose of vaccine, not only did not show harmful results, but began to mend shortly following the initial injection and recovered under daily injections of several times the usual adult dose. A second child with pneumococcus meningitis showed prompt diminution in the cerebro-spinal fluid and sharp amelioration of symptoms accompanying the use of four to eight times the adult dose of pneumococcus vaccine."

Dr. W. H. Watters, of Boston, has this to say on the subject: "In general septicemia of streptococcus origin, we have frequently observed distinct amelioration following the hypodermic administration of bacterial emulsions, both autogenous and stock. This is by no means universal, however, some apparently hopeful cases finally succumbing to the disease. In even these fatal cases we can usually note clinically an increased degree of resistance on the part of the patient with a correspondingly prolonged fight before finally overcome. It is in puerperal septicemia, however, in which some of our most satisfactory results have been obtained."

Harrower (Clinical Medicine, March 12, pp. 301, 302), in reply to some statements that vaccines are dangerous, brings out so many pertinent quotations that I will reprint the article in toto:

"Recently I had occasion to note, in the book-review department of the December number of your most excellent

journal (Clinical Medicine, December, 1911, p. 1340), some statements regarding the dangers of vaccine therapy to which I wish to take exception.

"You write: 'Vaccines have a greater possibility for harm than chloroform, morphine, strychnine, and other drugs of the kind. They are not dangerous in the hands of men who have studied their actions and the principles underlying their application, because then their administration is controlled.'

"While I have every respect for the abilities of the editor, and, too, for his clinical experience, I cannot but differ with him materially in this respect. To put it very plainly, vaccines are not dangerous. This statement is made with all due deference to the feelings of many whose articles or statements I have read or heard. I will qualify this statement by adding 'if properly used.' It must be evident that any agent, to be therapeutically valuable, must carry with it possibilities of harm if its use is overdone, just as too much bread or too much butter will make a man sick.

"It is a fact that there is as little possibility for harm in the bacterial vaccines as in any drug in the materia medica, and statements calculated to scare the profession are unfortunate, because vaccine therapy contains within it such tremendous possibilities for good. No step has been made in therapeutics during the past ten years that has been anything like as important as the work first done by Wright—no, not even salvarsan.

"The only way in which I can reconcile your statement is to suppose that you must be considering tuberculin as a vaccine, and, of course, as tuberculin is a toxic product and not really a vaccine at all (which latter are given in cases where the patient is already fairly saturated with similar toxins) the possibilities for danger from its careless or unwise administration are very great.

"Fortunately, the literature on vaccine therapy is becoming quite voluminous and covers practically every phase of this broad subject. I have collected a few excerpts from recent literature, which may serve to prove my contention, that vaccines, when used with the care that is possible by a physician who knows enough to know how to use drugs (even though he may know nothing about vaccine therapy), are not dangerous.

"Doctors Williams, Cragin, and Newell ('Transactions of the Congress of American Physicians,' Vol. 7, 1910, p. 160) say: 'As the ordinary localized puerperal infections, irrespective of the nature of the offending bacteria, tend to spontaneous cure, the field for vaccine therapy is practically limited to acute general infections, where it unfortunately appears to be of little value, and the most that can be said from the reports thus far available is, that its employment does no harm.'

"Dr. Henry O. Riek concludes: 'Fifthly, that, if used with reasonable care as to dosage, and especially as to asepsis, vaccine therapy is a harmless measure and carries with it practically no serious risks.'

"Drs. J. B. Deaver, J. C. DaCosta, and D. B. Pfeiffer make this statement: 'As a contraindication to vaccine treatment conducted in this manner, we can only mention one, namely, overwhelming sepsis. It is not rational to expect help in such a condition, and from the nature of the case it is possible to do harm by adding more toxin, though we have not seen an instance of this clinically.'

"Dr. W. R. Allen, London ('Vaccine Therapy,' third edition, p. 117), in referring to the treatment of pneumonia with vaccines, says, among other things: 'A weak, irregular, very rapid pulse, enfeebled constitution, low muttering delirium, dry, furred tongue, and sordes about the mouth are, of course, unfavorable signs; yet so marked has been the improvement, even after one injection, in two cases of this type, that no case is to be looked upon as hopeless.'

"Dr. John H. Mudgett (Medical Council, Jan., 1912, p. 7) writes: 'Finally, I desire to again emphasize the ease and facility with which bacterial vaccines may be used by the general practitioner; and also wish to state, from my own large experience and from information obtained from reading, my opinion, that the use of bacterial vaccines is as safe as the employment of any of the potent drugs of the materia medica. They should be used by every practitioner of medicine as an accessory to his methods of treatment.'

"Dr. J. G. Callison, discussing typhoid fever (Post-Graduate, July, 1911), declares: 'When given in therapeutic doses, such stock vaccines are without injurious effect, and do not interfere with other treatment.'

"Dr. R. H. Dennet (Post-Graduate, July, 1911) in referring to a case of typhoid fever, says: 'The case was a very desperate one, but after the use of the vaccine went on to a complete recovery. The large dose this patient received certainly did no harm.'

"Dr. James M. Phalen (Journal of the American Medical Association, Jan. 6, 1912, p. 11), after reviewing the literature on the subject of typhoid fever treatment with vaccines, says: 'All agree, however, that even in cases in which it causes no improvement, it has done no harm.'

"An interesting experience is related by Dr. Timothy Leary, of Boston (Boston Medical and Surgical Journal, October 1910), which is quoted in his own words: 'In general infections vaccines are harmless. This was indicated in a case in which, through error, 10 c.c. of staphylococcus pyogenes aureus vaccine containing 10,000,000,000 organisms were injected at one time, as an initial dose. No harm resulted. In a second case the same dose produced a temporary collapse, with prompt response to heat and stimulation.'

"To close: Bacterial vaccines are not dangerous—if rightly used. The average physician is passing by a splendid thing if he is not using these remedies as a routine. The knowledge required to use vaccines effectively is not hard to obtain, nor does it require more than a few minutes —perhaps an hour or so—and if there is danger, it lies more likely in not using bacterial vaccines when they are indicated."

CHAPTER III.

AUTOGENOUS OR POLYVALENT STOCK VACCINES.

In the discussion of vaccine therapy much controversy has arisen as to whether autogenous or stock vaccines should be employed. This is a very pertinent question and should be considered from the standpoint of applied therapeutics: the treatment of disease under the conditions met with in every-day practice. The end in view should be the humane one of relieving the patient, and not the merely intellectual one of striving for some impossible ideal of scientific precision.

Autogenous vaccines are prepared from the micro-organisms found in specimens taken from the infected area of the respective patient, while stock vaccines are prepared from selected strains of micro-organisms found in infections at large caused by the same species of germs. The advocates of autogenous vaccines contend that immunizing responses to pathogenic organisms are absolutely specific within each class, and that this principle of specificity applies with the same absoluteness to the several strains of a single species. They conclude that, unless a vaccine is of the exact identical strain which has caused the infection, no therapeutic response will be obtained, and that the only way to be certain that a vaccine absolutely corresponds to the infecting organism is to prepare that vaccine from the germs found in the infected area.

Advocates of autogenous vaccines have written so extensively and have been so insistent on the "unscientific character" of stock vaccines that a false impression as to the value of stock vaccines has been created in many minds. Those who have written most strenuously against them have had little or no experience with their use, basing their

convictions on pure theory. Now that an overwhelming amount of clinical experience has demonstrated the incorrectness of these conclusions it is hardly worth while to go back to an examination of the theories on which the conclusions are based and to ascertain where the fallacies lie. However, especially in the large cities, so often do the teachers and leaders of medicine insist on contradicting fact with theory that it may serve a purpose to reveal some of these fallacies. The idea of absolute specificity is based purely on serological tests. It has never been demonstrated, however, nor is it true, that agglutination is the only immunizing resource of the blood against bacteria; to the contrary, it is far more probable that important roles are played by other defensive factors. It should be remembered that antibodies in the blood may be present which we are not able to detect. This is clearly shown in typhoid immunization. A positive Widal would indicate the presence of antibodies after vaccine inoculation. But Burlingame (The Lancet-Clinic, April, 1915), in compiling the results from Widals taken after 1,116 prophylactic typhoid injections, says in part:

"During the blood examinations it was not at all uncommon to find the Widal positive one week, the next negative, and again positive at the third examination, and so forth"; and again he says: "The administration of vaccine at regular intervals produces a positive or a typical Widal, usually within thirty days in about 94 per cent of the cases. This blood-reaction is quite variable, and becomes negative with comparative rapidity. Although this reaction has disappeared in the majority of cases, clinical evidence indicates that the immunity continues."

Neither is it true that the various strains of bacteria belonging to one species are immutable, and consequently absolutely specific in immuno-production. To the contrary, the varieties of one species are very apt to change in accordance with the soil upon which they are located, either in the infected area or on culture media. It is even true that

one species of germ may, under appropriate cultural conditions, change into another species of germ to which it is closely related.

Rosenow (New York Medical Journal, Feb. 7, 1914) has converted the pneumococcus into the streptococcus and the streptococcus into the pneumococcus. He has also succeeded in converting the various types of streptococci into other types.

In our laboratory we have had strains so close to the morphologic boundary line between pneumococci and streptococci that the characteristic streptococci or pneumococci could be grown at will by simply changing the culture media.

There is, of course, truth in the contention that when a stock vaccine containing a number of different organisms is used, it may never be known with certainty which of the organisms was really responsible for the infection. From a scientific standpoint, it may be regretable that the physician who has cured a patient may ever afterwards be in doubt as to whether the infecting organism was the staphylococcus albus or aureus; but from the standpoint of clinical efficiency that does not make a particle of difference. A physician who, when called to a case of puerperal septicemia, delays the use of vaccine until the findings of the laboratory tell him whether the infecting organism is the streptococcus or the colon bacillus, may obtain this wisdom only at the expense of the life of the patient. It is much better, in my opinion, to use at once a stock vaccine containing both organisms, even if the doctor has to suffer ever afterwards the mental anguish of being uncertain as to which part of the vaccine did the curing. There would be some weight to the objections to a combined stock vaccine if the unrequired portion of it were of any real disadvantage. As a matter of fact it has been asserted that only the strain of

organisms contained in the vaccine which happens to correspond with the organism causing the infection possesses immunizing properties, and as this particular strain is only a small part of the entire vaccine injected, the dose is too small to be efficient. This contention does not hold good. As has been pointed out before, sensitization for the production of specific proteolytic ferments may be brought about by a surprisingly small dose of vaccine; and furthermore, it is not absolutely necessary to have in a vaccine the same strain of a micro-organism that is present in the infection to procure therapeutic immunizing responses. On the contrary, it is not an uncommon experience, in the treatment of chronic infections, to find cases in which autogenous vaccines were employed with indifferent results, while prompt improvement takes place after using a polyvalent stock preparation. Reaction is an important factor in stimulating immunizing responses. In chronic infections a certain tolerance appears to develop between the cells of the body and the infecting organism, and it is reasonable to believe that a vaccine prepared from a germ to which a tolerance has developed will not produce the same amount of reaction as a vaccine prepared from a virulent, type-true organism. The fact that infecting organisms often become attenuated or modified during the course of a chronic infection to such an extent that they no longer serve the purpose as an efficient immuno-stimulating organism must also be taken into account.

In preparing stock vaccines the possible difference in immunizing properties of different strains of micro-organisms is taken account of, the vaccine being made polyvalent by using a number of strains, growing them separately and then mixing them. The fact stands out prominently that extensive users of vaccine use stock preparations in all except a few selected cases and that the largest users of vaccine theraphy have comparatively little occasion for autogenous products.

Clinical experience shows that there is an overlapping in immunizing responses from the various strains of an organism; that vaccines from one strain have at least some immunizing influence over infections by other strains. I have repeatedly demonstrated, clinically, to my own satisfaction, that streptococcus vaccine inoculations have a beneficial influence on pneumococcus infections. Concerning the immunizing influence of the various strains of staphylococci, Dr. Martin F. Engman (Congress of American Physicians and Surgeons, 1910, p. 187) says:

"It is curious to note the great variety of lesions procured on the skin by these cocci, which, upon cultural identification, will at one time prove to be of the aureus type, and at another, from a similar lesion, of the albus type. We have for many years believed that the morphological differences in this group of cocci meant nothing in their chemo-tactic qualities; that the former were largely due to incidents of growth and environment, and that such a coccus from a boil may present no morphological differences from those from a bullous impetigo or pustular eczema. Working on this assumption we have in experimenting with stock vaccines purposely paid no attention to the variety of coccus grown from a case, and have used suspensions of the staphylococcus albus for the treatment of cases from which was grown the staphylococcus aureus with as brilliant results as if an autogenous vaccine had been used. This we have done time and time again. Polyvalent staphylococcic vaccines have in like manner been used with as good results. It is our experience, however, that the suspensions of the white coccus for general use are efficacious."

Having shown that the theoretical objections to stock vaccines are not sound, let me point out some of the practical difficulties in the use of autogenous vaccines. Doctors who use only autogenous vaccines do not employ them as regular therapeutic measures, but only as last expedients. Therefore, ailments that could be checked promptly if a vaccine were used early are allowed to run their course until they become so serious that vaccine therapy is often

useless. Only then, perhaps, a bacteriologist is called to prepare an autogenous vaccine. Autogenous vaccines are not easily prepared, requiring considerable time, experience and training such as are not always available. To procure a culture, send it to a bacteriologist and have a vaccine prepared, will involve a delay of from two days to a week; this especially in acute infections is irreparable. Finally, in making autogenous vaccines, important germs may be overgrown by less pathogenic organisms, and the sterilization by heat which must be employed in the laboratory is apt to injure the bacterial protoplasm to such an extent that the vaccine suffers in efficiency.

In acute infections, autogenous vaccines have no place, because these infections are due to the common pus cocci and can practically always be checked with the proper stock vaccine, used on a clinical diagnosis. The true place for autogenous vaccine is in those chronic infections which fail to respond to a few injections of stock vaccines and show the presence of some unusual varieties of bacteria. Here an autogenous vaccine made from that germ and added to a stock preparation will usually accomplish all that can be expected.

An editorial on "Vaccine Therapy" in the New York Medical Journal, August 16, 1913, reads as follows:

"There is at present much discussion concerning the theory and the practice of vaccine therapy, or, more correctly, bacterination. Much is said concerning stock and autogenous vaccines. Which shall be used? Can any benefit result from the stock variety?

"There can be no doubt that in many instances the introduction of bacterins has been followed by most favorable results. There are those who contend that the use of a mixed bacterin is equivalent to using a 'shotgun' prescription in the hope that some one of the ingredients may hit the mark. The analogy does not seem to hold. It is a very common occurrence to obtain several varieties of microorganisms when cultures are taken from infectious conditions. Shall autogenous vaccines of each be made and tried

separately, waiting several weeks to determine the action or lack of action, or shall minimum doses of each be given at once, with the hope of getting more prompt reactions? If we wait for the individual reactions the patient will have had a splendid opportunity to become much worse. Inasmuch as there do exist mixed infections, it would seem that there is a place for mixed vaccines."

Gilchrist (Congress of American Physicians and Surgeons, Vol. VIII, 1910, p. 164) on the use of staphylococcus vaccine in skin affections says:

"Autogenous vaccines were made at first, but later it was found that stock vaccines acted just as well, so the former were not often used."

Martin F. Engman (Congress of American Physicians and Surgeons, Vol. VIII, p. 191) in reference to the use of staphylococcus vaccine says:

"Stock suspensions we have found very reliable and can be used in most instances * * * Autogenous suspensions are indicated where 'stocks' fail."

Professor John O. Polak (Journal A. M. A., Nov. 22, 1911, p. 1739) in part says:

"Autogenous vaccines of a single strain have given me unreliable reactions. This, I think, can be explained by the fact that the coccus is attenuated in its strength and, after it has produced its first reaction, the leukocytes become more or less accustomed to the particular variety of coccus, and are less liable to effect a defense than when a vaccine of polyvalent strain is introduced.

"Mixed vaccines of reliable laboratories have given better results than when a single variety was used. This has been shown repeatedly in the blood-picture when an autogenous vaccine of single strain used in large doses, even up to 500,000,000, has failed to increase the leukocyte count or diminish the polynuclear percentage, the mixed vaccines of several strains have promptly produced a marked leukocytosis. Even colon bacillus infections, such as the infection of a pelvic hematocele by the colon bacillus, have yielded more promptly to mixed vaccines of polyvalent strains than when a single autogenous germ has been used.

"One characteristic which has been noted throughout all of our experience is that, even before any definite effect has been noted on the temperature, the well-being of the patient seemed to be improved by vaccine injection."

Dr. J. M. Van Cott (New York State Journal of Medicine, July, 1911, p. 320), after giving tabulated results of 74 cases treated with a mixed streptococcus, staphylococcus, and colon bacillus vaccine, says:

"Analysis of the table results in the following conclusions:

"First. Proper use of the polyvalent vaccine described above is not only harmless, but it is also of positive value in many cases of infection.

"Second. A stock vaccine containing virulent strains has the advantage over the autogenous vaccines of saving valuable time, and being available at any moment for physicians who lack the facilities for procuring autogenous vaccines.

"Third. Vaccination is useless if the patient be already swamped with toxine. The only hope in such cases is to eliminate the toxine by catharsis, and the Murphy drip, or, where the infecting organism is known, by the use of an anti-serum in conjunction with the vaccine.

"Fourth. Early vaccination offers the best prospect of success."

I have extensively used autogenous as well as stock vaccines and feel confident that future experience will fully justify my opinion that in acute infections stock vaccines, when given early, will give better results than autogenous vaccines.

Autogenous vaccines should be used in those comparatively rare cases of subacute and chronic infections in which stock vaccines have failed to give the desired results, when bacterial examination shows that an unusual organism is present.

The essential feature in making good stock vaccines is to carefully select the cultures, make them up while fresh and sterilize them just sufficiently to just kill the organism.

If a mixed vaccine should be given having streptococci, staphylococci and pneumococci where only a pneumococcus infection exists, the streptococcus and staphylococcus will have no effect save to raise the immunizing powers against these organisms. This is an actual advantage as it serves to fortify the individual against a later possible infection by these ever-present micro-organisms.

CHAPTER IV.

VACCINES IN EVERY-DAY PRACTICE.

Materia medica, though it represents the accumulated experience of thousands of years, offers us few drugs to which we can pin absolute faith in the serious maladies of life. When we have counted up the many palliative remedies and the half-dozen really curative agents at our command, we still feel abundant reason to regret the poverty of our medical armamentarium. On the curative value of drugs, Simon ("Infection and Immunity," p. 18) says:

"Wonderful progress also has been made in surgery. By its means countless lives have been saved which otherwise would have been doomed. But after all, surgical treatment cannot be regarded as curative treatment in the proper sense of the word; the surgeon may amputate a badly crushed limb or he may remove a diseased appendix, or a cancerous breast, but he does not cure the limb, nor the appendix, nor does he restore the breast to its original condition. The final repair, the healing of the wound, is accomplished by the animal body itself. The surgeon, however, is frequently placed in a condition where he can assist nature materially to accomplish a cure, and in this respect he is certainly more favorably placed than the internist.

"The latter may be a most skilful diagnostician, an excellent pathologist, perhaps, but he does not cure the disease with which he is brought into contact. He may in a measure influence some diseases by his directions for the general care of the patient, but, as a rule, the patient dies or recovers irrespective of his therapeutic efforts, in so far at least as these efforts are based upon ancient empiricism. Typhoid fever patients still pursue the same course which was so well described by the physicians of the middle ages; our pneumonia death rate is still what it was when the earliest records on the subject were kept, and is virtually the same for the millionaire in his marble palace, surrounded by doctors and nurses, as for the tramp who is cared for by the roadside by his brother tramps."

For this reason the announcement by Sir Almroth E. Wright of a series of true specifics for many of the most common and distressing diseases of the body—those due to the ubiquitous pus-producing micro-organisms—constitutes an epoch-making discovery.

Though there is undoubtedly a rapidly growing recognition of the usefulness of vaccines as therapeutic agents, they have by no means attained the wide employment to which their manifest advantage entitles them. This is due largely to the abstruseness and inaccessibility for practical purposes with which immunotherapy has been surrounded in the literature. There are in the publications so many abstract theories, speculative postulates, and technical mysteries that the practitioner of medicine has felt himself unqualified for dealing with the subject and has relegated vaccine therapy to the infrequent special cases which belong to the laboratory. Most of the writings on vaccine treatment found in text-books and medical journals have been produced by laboratory workers, and naturally are dominated by the viewpoints of the theorist, with all his requirements for exactitude and scientific procedure. This in itself it very commendable; but the danger of philosophical views is that, because of the failure to include facts or by the inclusion of erroneous premises, they may turn out to be as false as they seemed plausible.

For instance, much discussion has arisen whether bacterial vaccines, as specific agents for combating certain infections, can be scientifically employed on a clinical diagnosis, or whether a bacterial examination should always precede vaccine inoculations. Laboratory workers contend that a positive diagnosis in infectious processes can only be arrived at by making a bacterial examination and that in the interest of scientific therapy, treatment should not be undertaken until bacterial determinations have been made. This position appears logical, but does not stand the

test of critical analysis. To employ exact methods is desirable, if more definite results can be obtained through them; but when exacting methods serve no useful purpose and may even be a serious hindrance to attaining the desired end, they can certainly not be considered truly scientific. Science is classified knowledge, knowledge that is arranged or worked out so that it can be practically applied. True science does not sacrifice the end for the means.

If it is true that in every case bacterial examination must precede the administration of a vaccine; that only autogenous vaccines are effective; that the administration of a vaccine not absolutely identical with the strain of bacteria causing the infection is futile; and that the administration of a vaccine containing bacteria besides those causing the infection is fraught with danger—then bacterial vaccines have no place in the general practice of medicine. They belong purely to the laboratory man, who can isolate the particular disease-producer, make an autogenous vaccine, administer it with painstaking, scientific technique, and so feel sure that he hits the mark.

When diphtheria antitoxin first came into use, it was thought necessary to verify the clinical diagnosis by a bacterial examination before its administration. Such a practice is now known to be dangerous because a bacterial diagnosis involves enough delay in treatment to impair the results, and may be responsible for a fatal termination. Here the knowledge that diphtheria antitoxin is harmless in non-diphtheritic cases, and that early treatment is of great advantage, makes its administration on a clinical diagnosis more scientific than its use only after a bacterial examination. The same principle applies to the administration of bacterial vaccines. In many cases of acute infections delay in giving the vaccine will prolong the course of the disease or endanger the life of the patient.

From this it should not be inferred that bacterial examinations are unnecessary. Many times the microscope and culture tube offer the only means of arriving at a correct diagnosis, but I wish to emphasize that the clinical indications are usually sufficiently characteristic to determine the infecting organism for the selection of an appropriate vaccine.

The usual infecting organisms in most diseased conditions are well known. A comparatively small number of varieties of infecting organisms cause a great majority of the diseases commonly met with. In treating disease it is not so much the large number of organisms that confronts us, as the great variety of diseases that may be produced by a single species of infecting organisms. Clinical symptoms depend largely on the disturbance of the function of the organ which has become infected. The symptoms from a streptococcus infection of the appendix, kidney, heart-valve, joint, cerebral meninges, or iris, are entirely different, and yet the infection is the same, and from the standpoint of immunotherapy, the treatment would be the same. The streptococcus may thus infect almost any part of the body, causing a large variety of diseases, and what is true of the streptococcus is equally true of the staphylococcus and the pneumococcus. Some organisms confine their ravages more to certain parts of the body. The colon bacillus, for instance, causes infections more particularly in the abdominal viscera and pelvic organs, while the micrococcus catarrhalis and the Friedlander bacillus are principally found in the respiratory tract. Mixed infections by these various organisms in their favorite habitats are most common.

In applying therapeutic immunization, the fact that only a few species of organisms are responsible for most infections, and that mixed infections by these various organisms are common, should not be lost sight of. The recognition

of the characteristic symptoms produced by the various infecting organisms in certain disease conditions provides a rational basis for the selection of the suitable vaccine. When the infection is of such character that a culture can be procured, a bacterial examination to determine the exact character of the infection will in many instances be of advantage, but it does not necessarily follow that such an examination is absolutely necessary to obtain good results with the use of vaccines.

Specific infections by the tubercle bacillus, gonococcus, Bordet bacillus, typhoid bacillus and other organisms are sufficiently characteristic to indicate preliminary bacterin treatment until a positive diagnosis is arrived at.

Many disease conditions are also encountered in which the infection is so situated that a culture cannot be procured, and a bacterial examination cannot be made. By familiarity with the usual infecting organisms, the proper vaccine can usually be selected and employed with good results.

It has been suggested that only those physicians who are familiar with bacteriology and trained in laboratory work should practice therapeutic immunization with bacterial vaccines. Such a contention would only hold good where a doctor wishes to do his own laboratory work and make his own vaccine, but can certainly not apply to the general application of bacterial vaccines. There is no more reason why a doctor should be a trained bacteriologist to give a dose of streptococcus vaccine than to give a dose of diphtheria antitoxin or some other biologic remedy. He should have a general knowledge of how these preparations are made, but the technical knowledge belongs to the one who is trained in making them.

The essential element that counts for competency in a physician is his ability to discern clinical conditions and apply the appropriate remedy at the right time. In applying

the remedy it is necessary for him to know what results are to be expected and how to interpret them clinically. This ability is only acquired by diligent and close observation in actual practice.

To use vaccines intelligently, a general knowledge of bacteriology and active immunization should be obtained. With the amount of current literature published on this subject there is absolutely no reason why the general practitioner should not be in possession of such knowledge; if not, he can with a little trouble acquire it. Clinical experience and his knowledge of how to observe the results of applied remedies enables the general practitioner to readily take up the vaccine treatment and use it with results that are fully as good and sometimes even better than those obtained by technical workers with less clinical knowledge.

For reasons pointed out before, there are still many physicians who have had but little or no experience with the therapeutic application of bacterial vaccines. To adopt this method of treatment it is necessary to realize that the selection of the cases to "try them out on" is of very great importance. Many doctors have "tried out" vaccines in a few cases and, not seeing satisfactory results, concluded that they are of no value.

A number of factors enter into the therapeutic efficiency of a bacterial vaccine, and the disregard of any one of them may result in failure, just as the combination of all of them leads to success. The following are the chief causes of disappointments:

1. The vaccine may have been made from feeble and degenerated organisms, or have consisted of only a single strain of bacteria, so that it failed to sufficiently stimulate immuno-production. The best bacterins are made from healthy, virulent organisms and are highly polyvalent, so that the immunizing apparatus is aroused against the infection, intensively, and all along the line. For instance, in a

pure streptococcus infection, a polyvalent vaccine consisting of virulent streptococci taken from many sources often acts much better than a vaccine made from a single strain of streptococci, even if taken from the patient's own specimen.

In many cases in which autogenous vaccines fail, polyvalent stock vaccines succeed. This is partly accounted for on the theory that the system has become so accustomed to the particular strain of bacteria which it harbors that it fails to respond to a vaccine made from that strain alone.

2. **The vaccine may have been prepared so that injury of the bacterial protoplasm occurred, changing the protein so that it is no longer specific to the infection.** Heat sterilization, so often carried out in making bacterins in the private bacteriological laboratory, if carried to excess, may be responsible for inert vaccines.

3. **The vaccine may not have completely met the infection.** A straight pneumococcus vaccine will accomplish little in pneumonia in which the pneumococcus is associated with the streptococcus and the staphylococcus. One of the difficulties in the preparation of autogenous vaccines has been that in culturing the specimen taken from the patient the chief disease-producer may be overgrown by less important organisms. The first and foremost postulate, therefore, is to use a vaccine in which all the probable disease-producers are represented, even if it contains an unneeded species of bacteria; when such a bacterin fails to clear up an infection, bacterial examination will usually disclose the presence of some unusual organism. Careless, loose thinkers, who never have had practical experience with bacterial vaccines, have raised their voices in warnings against possible malign effects from combined vaccines, but the absurdity of such notions has been shown in a previous chapter.

Bearing the facts in mind, the use of a combined vaccine based on the character and location of the infection is rational as well as safe, and failure to take this into consideration explains many an unsatisfactory result.

4. **The vaccine may have been used with neglect of the other indicated measures.** Anatomical malformations such as deviations of the nasal septum must be corrected, pus pockets treated surgically. Local antisepsis, where practical, is essential in conjunction with constitutional immunization. Sound general treatment should not be neglected.

5. **The vaccine may have been used too late.** Given a good, appropriate vaccine, used early in acute infections, a favorable result may be confidently predicted. But delay proportionately lessens the chances of success. It has been argued that in acute diseases the immunizing apparatus of the body is already sufficiently aroused. If this were always true we would have no chronic cases and no infectious sequels in those cases in which the patient gets clinically well. But in the majority of cases the contrary is true. Nowadays when we find an endocarditis we inquire for a history of rheumatism and tonsil infection. More and more do clinical studies reveal the fact that an unsuspected infectious focus may give rise later on to very severe sickness. Since, therefore, the system is not adequately producing immunizing bodies in acute infections, the injection of bacterial vaccines into healthy tissues to aid sick tissues in the combat with the bacterial invaders is rational. Late in disease, the immunizing apparatus of the body may be worn out and incapable of response, or the bacteria may have established themselves in foci of such inaccessible character that a bacterial vaccine may prove futile. Do not hesitate or wait in acute infections—give vaccines as you do diphtheria antitoxin.

6. **Timidity in dosage and irregularity in administration may not have been avoided in the use of the vaccine, or it**

may not have been continued sufficiently long to thoroughly eradicate the existing infection. This applies particularly to old chronic processes where the first few injections may not accomplish perceptible benefit, such as old rheumatism, gonorrhea and the like. The persistent employment of vaccine, together with the usual measures, will with few exceptions eventually succeed.

Briefly summarized, a good combined vaccine, selected in accordance with the clinical or bacterial diagnosis, administered early, in sufficient doses, at proper intervals, under observance of the other indicated measures, is an effective remedy. In exceptional cases, where an unusual organism is present, an autogenous vaccine should be employed. When a bacterial vaccine fails, one or more of these postulates has been violated. If someone tells you he has used vaccines "without results," ask him if he has observed all these requirements!

The doctor who wishes to determine the therapeutic value of vaccines should start by treating acute infections during their early stages. Every practitioner knows about how long it takes for an average acute infection to run its course. If by using vaccines he can reduce the illness to one-half or one-third the usual duration, there is no longer any room for doubting their therapeutic value. And this can be determined in a few days or a week's time. In chronic infections, especially those due to pyogenic organisms of the respiratory tract, prompt results will be secured and for that reason these are also good cases to try out the vaccines. As the physician becomes more familiar with this method of treatment, he will gain confidence in its value and reliability.

The wide scope for the successful application of the vaccine treatment can only be appreciated by those having a large experience in its use. When we consider that most of our ailments have been traced to some germ, and that

the majority of the common ones are caused by a small group of organisms, the tremendous influence for good there is in this method of treatment can be appreciated.

The most prevalent ailments met with are caused by the pus group of organisms, staphylococci, streptococci, pneumococci, colon bacilli, and gonococci. Conventional treatment with medicines in these infectious processes is of little practical value. Such remedies are not curative agents. At best they only give relief while Nature effects the cure. Vaccines, on the other hand, are real curative agents because they stimulate the immunizing mechanism of the body and thereby hasten the establishment of an immunity.

The inability to successfully cope with these infectious processes has been one of the chief causes which have brought the medical profession into disrepute in the estimation of many well-meaning people, and undoubtedly is responsible for much of our quackery and many of the innumerable patent medicines.

These conditions exist because the regular profession heretofore has not been able to accomplish enough. Bacterial vaccines will in a very large measure supply this want and restore an increasing confidence in the virtues of the medical profession.

CHAPTER V.

DOSAGE IN VACCINE THERAPY.

No feature of vaccine therapy is more mooted than the question of dosage. Wright was the first one to demonstrate that exceedingly small doses of killed micro-organisms were required to stimulate antibody production, and it was through his work that a regular system of dosage was established; but, while the dosage in general is fairly well settled, there is still considerable difference of opinion as to the exact size of the dose and frequency of inoculation. Some advocate the use of small doses and report good results, while others contend that large doses are necessary to obtain the best results. The range of dosage recommended ranges from five to ten millions to several thousand of millions of germs of the same variety. Streptococcus vaccine is recommended in doses ranging from 5,000,000 to 200,000,000; staphylococcus vaccine from 100,000,000 to 1,000,000,000, and so forth. To a casual observer, it may appear that remedies, the dosage of which varies so widely, must have indefinite effects, results that are not readily recognized. Drugs that require accurate dosage to produce certain definite effects have been employed so long in the treatment of disease that it becomes difficult to understand why practically the same results are often obtained with doses of non-drug remedies that vary ten to twenty times in size. Morphine given in one-eighth grain dose will show physiological effect, and even five times this dose produces poisonous symptoms.

In considering this question it should be realized that the therapeutic effect of a vaccine is in no respect a drug action, and principles of dosage that would apply to drugs can in no way apply to vaccines. Vaccines are given in such small

doses that drugs given in similar quantities would have absolutely no appreciable physiologic effect. Ten million germs weigh approximately 0.000,034 gr. and a dose ten times larger, namely 0.00034 gr., still represents an infinitesimal amount. So it may be seen that when we calculate doses by starting with such extremely small amounts, they may be multiplied 5, 10, 20 or even 50 times and yet remain extremely small.

From the fact that bacterial vaccines are employed in such small doses, it may be inferred that they are extremely toxic in their action, when injected into the body, and that large doses might have dangerous poisonous effects. This question has been thoroughly worked out on lower animals where it has been shown that large doses may be given with impunity. In my own work I have repeatedly given guinea-pigs proportionately from five to ten thousand times the usual dose given to man without ill effect. Vaccine inoculations exert their influence by starting cell activities in the direction of expelling an intruder that possesses the essential characteristics of a dangerous infection. The tissue cells are not aware that the injected germs have been killed and accordingly get just as active in their disposal as if a real infection existed at the point of the vaccine inoculation. The faculty of self-preservation against infecting organisms of necessity is highly developed, so that but a small quantity of killed germs is required to start cell activities in the development of specific enzymes, ferments or antibodies for the purpose of disposing of living germs. When tissue cells have once acquired this faculty of producing specific enzymes, they, by habit, continue to do so for some time after the infecting organism, represented in the vaccine, are disposed of and it is for this reason that small doses of vaccine may produce just as good results as larger ones.

REACTION A GUIDE.

The quantity of vaccine injected does not necessarily determine the amount of antibody production. This depends entirely on the amount of sensitizing influence the vaccine has on tissue cells. The amount of vaccine necessary to effectively sensitize tissue cells for specific enzyme production holds a position within certain well-defined limits, inside of which there is considerable room for variation. The amount of local inflammatory disturbance which develops at the point of inoculation, coupled with a possible constitutional reaction of slight fever or malaise, is a good index to follow in determining dosage. It is necessary to avoid giving a dose sufficiently large to cause intense disturbance, because experience shows that when much inflammatory reaction develops at the point of inoculation the therapeutic results are not as marked as when the dose is sufficiently small to cause but moderate reaction. It seems that very severe reactions have a certain devitalizing influence which hinders specific proteolytic enzyme production to full capacity. On the other hand, a dose may be so small that it will make no impression and consequently be of no therapeutic value. Furthermore, the susceptibility of different individuals to vaccine inoculation varies much; the dose that would cause much reaction in one person would cause no disturbance in another. For this reason, it is advisable to start treatment with a small dose and work up in accord with the reactions, therapeutic effects and symptoms which each individual develops. The greatest amount of reaction usually follows the first inoculation and it becomes less with subsequent injections under increasing doses. In determining dosage, however, it is necessary to make a distinction between chronic ailments and severe acute infections; doses given to advantage in chronic ailments will not be adequate in severe, acute cases.

What Causes the Reaction?

In chronic infections, tissue cells are in a sense quiescent to the extent of tolerating an existing infection. In view of the general ill health which usually accompanies localized chronic infections, there is good reason to believe that devitalizing germ products are absorbed from the infected area which have a tendency to keep tissue cell activities of the entire body below par. At all events, when vaccines are injected into the healthy tissues in such cases, comparatively small doses cause considerable local inflammatory disturbance at the site of injection and not infrequently constitutional reactions as well. Vaughan and others would attribute this tendency to reaction in cases of chronic infection to a condition of anaphylaxis; the existing chronic infection, they believe, has sensitized the patient so that enough specific proteolytic ferments are present in the blood to disrupt the protein molecule contained in the killed micro-organisms constituting the vaccine, and the poisonous radicle of the germ protein, being thus liberated, rapidly causes the development of this reaction. This explains the situation theoretically; but it does not account for the fact that the reaction occurs when vaccines are inoculated into perfectly healthy individuals, as in the application of vaccine for prophylaxis. In anti-typhoid inoculations we find that more reaction develops from the first small dose than from the subsequent two larger doses. The same rule holds good with vaccines for the prevention of whooping cough, meningococcus and other prophylactic inoculations. If the reaction in chronic infections were due to specific sensitization and the action of proteolytic ferments on the inoculated organisms, we should expect more reaction to develop from the second and third prophylactic vaccine inoculations than from the first; because, by the time the second and third inoculations are made, at least some sensitization for the production of specific proteolytic ferment toward the inocu-

lated organism has developed. But on the contrary we find less reaction under increasing doses, identically the same condition that prevails under repeated inoculations where vaccines are employed for therapeutic purposes.

THE REAL CAUSE OF REACTIONS ELUCIDATED BY BESREDKA.

The development of sensitized vaccines throws some light on this subject. Besredka has demonstrated that when pathogenic micro-organisms are suspended in immune blood serum, certain immune bodies link or combine with the germs and that when these germs are then injected into man less reaction develops, even when much larger doses are employed. The purpose of making vaccine inoculations is to sensitize the patient to the organisms contained in the vaccine so that the antibodies formed as a result of this sensitization will destroy the corresponding organisms in the infected area. Chronic infections exist because a sufficient sensitization with the development of specific proteolytic ferments to destroy the germs in the infected area has not taken place. Reaction, tissue protest, is the essential factor which establishes this sensitization. In the unsensitized, whether in the presence of a chronic infection or otherwise, it requires but a small amount of vaccine to produce a reaction, to arouse a protest. As a result of this sensitization, antibody, specific proteolytic ferment is produced. This immunizing substance, by means of the circulating blood, is conveyed to all parts of the body and becomes a part of the body fluids. Upon reinoculation, antibodies that have developed as a result of the previous injections will link with or hitch to the micro-organisms contained in the vaccines in the same manner, as Besredka's experiments demonstrated, as when germs are suspended in immune serum; in the one instance, the germs become "sensitized" in vivo, while in the other, the same process takes place in vitro. This accounts for the fact that as

immunizing responses develop, larger doses of vaccine are tolerated without the same amount of reaction. It also explains a clinical condition which I have observed many times in the treatment of chronic infections with autogenous as well as stock vaccines. When the patient, upon repeated inoculations, remains sensitive and reacts markedly to small doses, not much, if any, improvement takes place in the infected area. This would indicate that not much antibody formation takes place as a result of the inoculations; consequently, the germs contained in the vaccine on reinoculation do not become sensitized.

Are Sensitized Bacterins Preferable?

In passing, we may take up the question as to whether sensitized vaccines are preferable to unsensitized bacterial suspensions as therapeutic and prophylactic agents because they produce less reaction, which has, during recent years, received considerable attention in medical literature. Logically, the advantages are not apparent. Vaccine inoculations are made for the purpose of hastening the establishment of an active immunity. To accomplish this a certain amount of reaction appears necessary though severe reactions should be avoided. The stimulating agent should have the characteristics possessed by the infecting organisms to bring forth a specific protest or reaction. Unsensitized killed micro-organisms certainly conform more closely to these requirements than sensitized killed ones do. In their therapeutic application, sensitized vaccines are given in much larger doses than the unsensitized. This would indicate that organisms previously loaded with antibodies are not as active an antigen to stimulate antibody production as the usual bacterial suspensions are, and consequently to obtain equal results a greater number of organisms must be injected. From the clinical literature on this subject there is no indication that sensitized vaccines are better

immunizing agents, either therapeutically or prophylactically, than unsensitized vaccines, and theoretically the unsensitized variety should be more efficient in establishing a lasting active immunity.

DOSAGE, MINIMUM AND MAXIMUM.

The range of dosage usually employed in giving bacterial vaccines for therapeutic immunization in diseases caused by the usual infecting organisms may be formulated as follows:

Organism	Minimum Dose	Maximum Dose
Streptococcus	20,000,000	250,000,000
Pneumococcus	30,000,000	300,000,000
Staphylococcus Aureus	100,000,000	1,000,000,000
Staphylococcus Albus	100,000,000	1,000,000,000
Colon Bacillus	60,000,000	400,000,000
Gonococcus	50,000,000	1,000,000,000
Typhoid Bacillus	100,000,000	1,000,000,000
Friedlander Bacillus	100,000,000	400,000,000
Micrococcus Catarrhalis	100,000,000	400,000,000
Acne Bacillus	5,000,000	50,000,000
Influenza Bacillus	100,000,000	400,000,000
Bordet's Bacillus	100,000,000	1,000,000,000
Pseudo Diphtheria Bacillus	100,000,000	400,000,000
Non-virulent Tubercle Bacillus (special)	100,000,000	1,000,000,000

Bacterial vaccines are usually prepared to contain a certain number of micro-organisms per cubic centimeter, and when more than one variety of organisms is employed to make mixed vaccines, the number of each variety of organisms is designated per cubic centimeter. With a syringe graduated in tenths of a cubic centimeter, the required dose may readily be calculated. When a syringe graduated in

minims is employed, the required dose may easily be computed by allowing about sixteen minims to represent one cubic centimeter. In making vaccine inoculations, the usual aseptic precautions should be observed.

Dosage in Subacute and Chronic Infections.

In the treatment of subacute and chronic infections, the first dose should be gauged so as to serve as an index for the size of subsequent inoculations. There being considerable difference in the susceptibility in different individuals, it is always advisable, in such cases, to start with a small average dose. A moderate amount of inflammatory reaction about the size of a dollar at the site of inoculation should be looked for inside of 24 hours. The next inoculation should be withheld until this inflammatory reaction has subsided, which usually requires from four to seven days; then a somewhat larger dose should be given, from which a similar reaction may be expected. If less reaction should develop from the larger second dose than took place after the first inoculation, the amount may be rapidly increased to a full dose, which ordinarily amounts to about one cubic centimeter of vaccine. After the first three or four inoculations, but little if any inflammatory reaction will develop, and meantime clinical indications should show rapid improvement. In many instances all symptoms of infection will subside after two or three inoculations, but it is always advisable to make a few more inoculations at somewhat longer intervals to insure permanency of result. When, in chronic cases, improvement does not take place so rapidly, treatment should be continued over a long period of time, for a number of months or possibly a year, making inoculations at from five to seven-day intervals. Crowding the treatment by giving very large doses or by making short intervals the rule is only exceptionally of advantage. Often after having continued treatment for some months it will

be found of advantage to give the patient a rest by discontinuing treatment for three or four weeks, and then resume treatment. By careful, patient, persistent treatment, an immunity can often be built up where either insufficient or too persistent treatment would fail.

If an extensive inflammatory reaction should develop after an initial dose, covering an area half the size of a hand or more, with slight fever and malaise, the dose was larger than necessary, and consequently the subsequent dose should not be increased. If a similar reaction should develop from the second inoculation, the third dose should be somewhat smaller and treatment continued with a similar small dose until a tolerance or immunizing resistance to the vaccine has developed, when the amount may be gradually increased to the usual dose. In this class of cases, inoculations should be made at weekly or ten-day intervals and sometimes even farther apart.

DOSAGE IN ACUTE INFECTIONS.

In the treatment of extensive acute infections with high fever and toxic symptoms we find from experience that treatment may be started with full doses, usually one cubic centimeter; that as a rule very little reaction develops either at the point of inoculation or constitutionally, and that inoculations may be made to advantage at one or two-day intervals and, in extremely severe cases, even twice daily for one or two days. After the more acute symptoms have subsided, as shown by a reduction of temperature, and other indications of improvement have set in, the interval between inoculations should be extended to two or three days, and during convalescence to weekly intervals for several weeks.

When employing vaccines in the treatment of the less severe localized acute infections, where there is slight fever and very little constitutional symptoms, the initial dose

should be smaller, because in such cases large doses are liable to produce marked reactions, but inoculations may be made to advantage at one or two-day intervals, while the dose is increased as indicated by the amount of reaction which develops from the previous inoculations.

Early Treatment.

In all acute infections, early treatment is of paramount importance, of greater importance than an exact bacterial diagnosis. Where delay in treatment would be entailed by procuring the exact vaccine indicated in a particular case and a mixed vaccine is at hand which contains as one of its constituents the micro-organism indicated in the case under treatment, such a vaccine should be employed until the one desired can be procured.

CHAPTER VI.

THE GENERAL TONIC INFLUENCE OF VACCINES.

Tonic effects have been ascribed to many remedies and methods of treatment and the term has been somewhat loosely applied. Generally speaking, any agent that aids in building up the system is a tonic. This applies to the increase in healthy metabolism with augmented cell activity. Many measures in common use have this stimulating effect, among them being wholesome exercise in the open air, the influence of sunlight, properly applied hot or cold baths, massage, electric radiation, etc.

In our scientific age, in which the spirit of inquiry dominates everything, we are never quite satisfied with our methods of procedure unless they are supported by some tangible explanation of their action. In the treatment of disease, however, this is often very difficult. The therapeutic value of bacterial vaccines is ascribed to their specific immunizing influence on an infection corresponding to the organisms contained in the vaccine, but results are also observed that cannot be ascribed to this specific action alone. Dr. Bloch (Correspondenz-Blatt für Schweizer Aerzte, Basel, October 31, 1914, No. 44, pp. 1377-1392) had marked success from giving gonococcus vaccine intravenously in toxic doses for gonorrheal arthritis, epididymitis and prostatitis. It occurred to him that probably the severe reaction obtained was mainly responsible for the therapeutic result. He accordingly gave three cases of severe gonorrheal rheumatism intramuscular injections of typhoid vaccine, and effected a cure in all three cases. Evidently these results were not due to any specific immunizing influence to the gonococcus and can more reasonably be accounted for on the ground that the typhoid vaccine stimulated cell activi-

ties of a tonic character such as sometimes follow acute intercurrent diseases where, after recovery, old chronic infections are also cured.

Bloch's experience argues in favor of the employment of mixed vaccines; to say the least it certainly would indicate that the giving of a vaccine containing organisms to which no corresponding infection exists, can do no harm.

A large majority of extensive users of vaccine prefer the mixed preparations because experience teaches them that they give the best results, and in all probability this is due to tonic activities besides the specific immunizing properties of the vaccine.

I. M. Mullick, M. A., M. D. (Calcutta Medical Journal, Aug., 1911, p. 41) gives a detailed report of the increased metabolic activity in a variety of cases, as indicated by increased elimination in the urine during the 24 hours. In part he says:

"These facts certainly give us some light as regards the changes within. Very probably it is this: (1) That vaccines stimulate metabolic activity, increase elimination of waste and rebuild tissues. (2) That they hasten catabolism, especially of weak and unhealthy tissues and help the building or regeneration of the healthy ones. In other words the tissue cells are influenced in such a way that they change rapidly, break down where they are weakest and regenerate in a more normal and healthy way. As already said I have similar records of many such cases, although the records are not always so consistent on the whole, it may be affirmed that vaccines stimulate metabolism.

"Even in old people this is evidenced; but in the young with their tissues in a higher state of vitality, this vital response is the most marked. Now, one very important bearing that this has is its general applicability and usefulness in all diseases, and in convalescence as a secondary help. Especially in this latter case such treatment may probably materially help convalescence by enabling the system to better eliminate effete material and toxins, and at

the same time by a better regeneration of tissue and body weight. For this purpose any mild and innocuous vaccine will do, preferably staphylococcus which is the commonest and the most mild to man.

"Summary and conclusions—I. Vaccine injections have a profound and favorable influence on metabolism. They increase the elimination of waste and at the same time tend to cause an increase in body weight.

"II. This metabolic aspect of vaccine therapy is as important a study as the others—its phagocytosis, opsonins, agglutinins, precipitins, etc.

"III. Different methods of preparation are useful for different purposes—the medium, sterilization, dosage and mixed vaccines.

"IV. Besides the specific action, vaccine inoculations improve the general condition by inducing a healthy metabolism as mentioned above.

"V. Hence it is useful in diabetes, malassimilation of invalids. Proteid nourishment, oxygen, and elimination of waste matter helps the efficiency of vaccine."

Dr. V. Dabney (New York Medical Journal, Feb. 10, 1912, pp. 275) proposes a plausible explanation of the tonic effect of vaccines on Ehrlich's side chain theory: "The limiting of the spread of infection was observed as one of the effects of vaccines in throat cases; so here, where the infections are more prone to linger, and the elaborated toxins to become absorbed, is exhibited more prominently the striking effect on metabolism. Bruce invited attention to the remarkable effects of vaccine therapy in building up the physique of patients suffering from chronic mania, in whom lack of nutrition is so often a prominent symptom. The same corrective tendency is to be found in the treatment of chronic middle ear diseases. However, this is not to be accounted for solely by the cessation of the suppurative process, as metabolic changes are slow ordinarily after the local lesion ceases to poison. In long suppuration of the middle ear, and in stubborn sinuses following the various mastoid operations, there is encountered often a septic condition, almost a cachexia, in a patient, whose anemia, depleted vitality, and loss of appetite are familiar to all otologists. The speedy correction of this untoward state and the cessation of the pus formation are, under vaccine ad-

ministration, the results of one and the same process, so brilliantly exploited by Ehrlich in his side chain theory. In brief, the receptors previously having in health the function of uniting with a food molecule and assimilating it, under disease conditions unite with a molecule of toxine, thus shutting off that much nutrition from the body. Naturally when the toxines are numerous, numerous receptors are pre-empted by them, and the metabolism of the body suffers proportionate detriment. Thus destroying these toxins, the vaccine renders available for food assimilation receptors heretofore occupied with toxine assimilation. The apparent effect of vaccine therapy on metabolism seems to bear out this theory.

"From the fact that pathogenic bacteria are more or less with us at all times it is fair to assume that at least some of them have a stimulating influence on metabolic activity. In actual life it is not an uncommon experience to find children or even adults, where an undertone of vitality existed for years, develop robust health after recovering from some infectious disease. No doubt even in a condition of health the immunizing faculty of the system is often called into activity to guard off infecting organisms without the individual becoming aware that an infection exists and in all probability these repeated slight immunizing responses are to a large extent responsible in sustaining an immunity and a normal standard of vitality."

This tonic effect of bacterial vaccines has not received enough attention. A tonic in all likelihood exerts its influence by stimulating cell activities through a certain kind of cell irritation. The tonic property of arsenic is probably due to cell irritation and the same properties may reasonably be ascribed to other tonics. That a patient is often in better condition after recovery from an acute infectious disease than before sickness, is a common experience. Recoveries from typhoid fever are good illustrations. The most rational way to account for this is that as a result of the infection, tissue cells have been stimulated to activities and that these activities continue for a considerable length of time after the infection has subsided. By giving a vaccine,

cell activities identical with those that take place during an infection are aroused; but the germs in the vaccine being dead, the benefit of these activities may be obtained without the dangers of the disease incidental to infection with a live organism. Furthermore, complement fixation tests and clinical experience have invariably shown that a more marked immunizing response is obtained from a vaccine inoculation than from an infection. This demonstrates the marked influence of a vaccine on tissue cell activities. After a vaccine injection we find an increased number of leukocytes in the blood, and subjectively there is an increased desire for food, active digestion and assimilation, associated with a feeling of general well being. This can be experienced by any one who will take two or three average adult doses of a vaccine at three or four-day intervals, even when he is presumably in good health.

In our dealings with diseased conditions it is essential that our measures conform as nearly as possible to nature's methods. Our close association with certain infecting organisms would at least indicate that they constitute essential factors to our well being and that stimulating cell activities to increased vitality is one of these. Vaccines which contain the most common infecting organisms serve this purpose best. A combined vaccine containing colon bacilli, streptococci, pneumococci and staphylococci is the one usually employed. Bacterial vaccines consist essentially of bacterial proteins and are given in such extremely small doses that no harmful results can follow their administration. Being proteins, they are entirely decomposed by the tissue cells of the body; nothing of a toxic character, similar to alkaloids or mineral poisons which are often used as tonics, remains for elimination—a decided inherent natural advantage over the employment of drugs.

Digestive disturbances are always a prominent feature where the general vital powers are depressed. Not infre-

quently we are consulted to prescribe for a case in which about the only complaint is a feeling of lassitude. The patient has no desire to take food and is never hungry. Examination may not reveal any definite diseased condition nor irregular habits of life. In such cases a course of six or eight inoculations of mixed vaccine, extending over a few months' time, will work great benefit, and the significant feature of this treatment is that improvements thus obtained are permanent.

In treating chronic diseases I have often noticed that a feeling of general good health with an increased appetite is the first indication of recovery. This has been particularly observed in cases of chronic arthritis, neuritis, and chronic catarrhs. In such cases I have often found myself wondering whether it was the immunizing or the tonic effect of the vaccine that was the most important.

This general tonic effect of vaccines may be applied to advantage in many instances where other remedies fail. From this it should not be inferred that vaccines will do everything. I frequently find that in anemic cases the response to the vaccine is slow but if in such cases the vaccine is given in conjunction with the hypodermic or intravenous use of some iron preparation the results are better than when either the vaccine or iron are used alone. The same is true with regard to other therapeutic measures known to have a tonic effect. The vaccines will not interfere with any other remedies used but will aid them. I have used vaccines extensively in this way and feel confident that much good can be accomplished with them.

CHAPTER VII.

INFECTIONS OF THE NOSE, THROAT AND ACCESSORY SINUSES.

General Considerations.

Most infections take place by microbic invasions of mucous membranes. The mouth and respiratory tract offer an extensive area of mucous membrane which is constantly exposed to attack by germs that may be present in the inhaled air or adhere to partaken food, and this makes infections of this part of the body most common. In fact, a large portion of the minor ailments met with in everyday practice and many serious diseases as well have their origin in the nose, throat or mouth. Acute rhinitis, pharyngitis, laryngitis or tonsillitis may be regarded as a trivial affair which usually subsides sooner or later without serious consequences, but dangerous extensions of infections from these small foci take place entirely too often to justify our neglecting them from the standpoint of immuno-therapy.

In a patient who for some time has complained of slight fever associated with an erratic heart action, endocarditis is at once suspected, and if verified the trouble is usually traced to a tonsillitis of similar infection. The same may be said of rheumatic fever. Mastoid infections and otitis media with few exceptions have their origin in the throat. Sinus infections also have their origin in extensions from the nasal mucous membrane. Bronchitis and bronchopneumonia follow "colds," and lobar pneumonia has the same origin. The clinical history in cases of nephritis often shows that the disease had its origin with a "cold," when infecting organisms unquestionably gained entrance to the general circulation and caused metastatic infections involving the kidneys. Gastric ulcers in all probability are also due to metastasis produced by germs that gained entrance

to the circulation from localized infections of the mouth or respiratory tract. When infections in the mouth, nose or throat exist a large number of the germs are constantly swallowed and may start localized infections in the various portions of the digestive tract.

The danger of extension of the infection can not be reckoned by the clinical appearance of these cases during the early acute stages. Many cases of severe rhinitis, pharyngitis or tonsillitis will subside spontaneously in a comparatively short time, while less severe cases may linger for a longer period or subside and leave serious infective processes in other parts of the body. This fact was most forcibly impressed on my mind a few years ago under the following circumstances: My son, while transplanting influenza cultures, found that he was out of rabbit's blood, and consequently used some of his own blood for the cultures. The next day he found all his influenza cultures contaminated with a pneumococcus. The only way to account for this was to conclude that he must have a pneumococcus infection of his blood. To verify this, cultures of his blood were carefully prepared on agar slants and every culture developed colonies of pneumococci. He was apparently well except that he had had a slight rhinitis for several days. There was no fever or other toxic symptoms. Vaccine treatment was instituted at once and in less than a week's time the blood was free from this organism. In all probability, if vaccines had not been given this would have developed, in a few more days, into a case of lobar pneumonia, from a localization of the infection in the lung. Such cases point out the necessity of considering infections, however slight, as conditions with dangerous possibilities which should always be treated accordingly. Here the infection in the nose was not sufficiently severe to make immuno-therapy seem necessary and had it not been for the accidental discovery of the pneumococcus in the blood,

vaccines in all probability would not have been given until a serious illness had developed. If vaccines had been given at once for the rhinitis, enough immunizing resistance would have developed so that blood invasion by the pneumococcus would not have taken place.

Chronic local irritation of mucous membranes, especially of the mouth, throat and digestive tract, is well recognized as an etiologic factor in cancer development. That localized irritation is always associated with infections by pathogenic micro-organisms can hardly be questioned. But it makes little difference whether an inflammatory process is started by mechanical or chemical irritation; it is the infective processes which follow the local disturbance that become the main irritating factor. There is nothing which so persistently keeps up tissue irritation as a chronic low-grade infection. That local treatment with antiseptics is largely inefficient in these localized infections is clearly evident from the many failures of this method, and where strong antiseptics are persistently used there is reason to believe that the local remedy has an irritating instead of a healing tendency.

Statistics show that, of the various forms of chronic infections associated with cancer, pyorrhea is the most common, especially where the cancer develops in the alimentary canal. Cancers of the liver, male and female generative organs, are always preceded by chronic infections.

Lawson (Journal of the National Medical Association, January-March, 1915), after reviewing the work done by various investigators, sums up the situation in part thus:

"1. That apart from the sexual organs 86 per cent of all cancers occur in the alimentary tract.

"2. That long-standing chronic inflammation in the sexual organs, and in other parts of the body, is known to predispose to the development of cancer.

"3. That the great majority of persons suffering from cancer in the alimentary canal have pyorrhea alveolaris which has been present many years.

"4. That this peridental disease is not nearly so common in persons not suffering from cancer.

"6. That the majority of cancers of the stomach show a history of chronic gastritis of many years' standing."

"5. That 'pus-eating' brings on gastritis.

If these deductions are correct, efficient treatment of infectious processes will necessarily have a far-reaching influence in preventing the development of cancer. Much stress is laid on the necessity of early operations where cancer is suspected, but efficient treatment to prevent cancer development is still better.

All infections are acute before they become chronic, and from our experience in the treatment of localized acute infections with bacterial vaccines the results have been sufficiently uniform to warrant the assertion that exceedingly few cases of infection will become chronic when vaccines are used early. And even in chronic infections, if the vaccine treatment is persistently followed up, good results are obtained in a large majority of cases.

The possibility of avoiding cancer development by applying immuno-therapy in localized infections of mucous membranes is too important to be neglected.

Acute Rhinitis, Pharyngitis, Laryngitis.

Among the common ailments met in general practice, acute infective processes of the upper respiratory tract respond most promptly to vaccine therapy. Few escape rhinitis, pharyngitis, laryngitis, "colds," but results from the use of medicines are so disappointing that comparatively few people consult a physician when thus afflicted. The impression that "nothing can be done for a cold" is quite prevalent because no definite method of treatment for these cases has been adopted by the medical profession as a whole. This inefficiency in the treatment of minor ailments has lowered the medical profession in the estimation of

many well-meaning, intelligent laymen. The argument is often advanced that if a doctor can not cure so trivial an ailment as a cold, how can he accomplish anything when confronted with a serious disease. Naturally the physician who is able to give prompt and efficient relief when called on to treat minor ailments soon gains the confidence of his patients in the more serious troubles; and what is true of this esteem toward the individual physician applies equally to the medical profession at large. Probably 75 per cent of the prevailing infectious diseases are simply tolerated by the laity until spontaneous recovery takes place; often the infection, meantime, becomes chronic, being unaided by a physician, simply because nothing sufficiently tangible is offered to warrant taking the treatment. Most people have found that throat lozenges or rhinitis tablets, at a cost of 5 or 10 cents, will give about as much relief as a prescription by the family physician, but we all know how sadly inefficient these remedies are. If efficient treatment were administered these neglected ailments would be regularly taken care of by the medical profession, to the enormous benefit of the general public. Few people would tolerate a "cold" if they were aware of the prompt relief and efficient cures that may be obtained from the injection of bacterins by their physician. These so-called "colds" are now generally recognized as infections of the upper respiratory tract, pneumococci, streptococci, the micrococcus catarrhalis, Friedlander bacilli, influenza bacilli, and other organisms being found. Usually there is a mixed infection of two or more of these. Of these the most common and persistently pathogenic are the pneumococcus and streptococcus.

The micrococcus catarrhalis and the staphylococcus are practically always present in chronic catarrhs, while the Friedlander bacillus and the influenza bacillus are not so often found.

While acute pneumococcus and streptococcus catarrhs or inflamed throats are with us more or less constantly, there are times when they become distinctly more prevalent and when the types of the infection are more severe. Furthermore, these infections frequently run in cycles; distinct epidemics of a certain organism spring up which die out and are followed by some other organism. Infections of the nasal sinus by the more virulent types of pneumococcus usually cause sufficient irritation to develop blood-streaked mucous discharges from the nose. Severe streptococcus infections of the nose are not so common, but this organism is more liable to cause severe inflammation of the nasopharynx, tonsils and larynx. Sometimes, for a while, the Friedlander bacillus is a predominating factor in these acute colds, then again the micrococcus of catarrh may take its place. Influenza bacillus infections prevail in distinct epidemics.

When these acute epidemics die out the infection has a tendency to become subacute or chronic in a certain percentage of cases when immuno-therapy is not instituted, in which the streptococcus and pneumococcus almost invariably are the important pathogenic factor, mixed infections becoming the rule. Some individuals suffer from these colds frequently and severely, while others are more fortunate and have mild attacks at longer intervals. The reason so many people have repeated attacks is because the system is not sufficiently impressed by the invading organism during the attack to make the immunity lasting. In this class of cases we have essentially a surface infection on a mucous membrane largely overlying bony structures with a small amount of submucous connective tissue. There is good reason to believe that sensitization for antibody or specific proteolytic ferment production is primarily dependent on the tissue cells involved in the infected area. Necessarily the amount of tissue involved in such cases is but a

small fraction of the entire body. Estimating the nasal mucous membrane with the submucous tissue as a sixteenth of an inch thick, it would require sixteen square inches of membrane to make a cubic inch of tissue. Immunizing responses resulting from such a small amount of tissue involvement are not liable to build up an extensive systemic immunity to protect against future attacks; and besides, when we consider that the live organisms causing the infections are not good antigens to stimulate antibody production from their devitalizing influence on the involved tissue it can readily be seen why infections of the upper respiratory tract are so liable to relapse and become chronic. Here is where vaccine therapy comes to the rescue. By bacterin inoculations of healthy tissues of the body, idle tissues are exploited for immuno-production with an efficient antigen that does not have a devitalizing influence on the tissue cells while they are becoming sensitized for antibody production, and consequently by repeated inoculations a systemic immunity is developed which makes subsequent infections of comparatively infrequent occurrence.

When these cases are treated with autogenous vaccine it is not advisable to use a vaccine prepared from a certain culture for a considerable length of time, because the bacterial flora may change. Not infrequently it is found that where good results are obtained from an autogenous vaccine that was prepared from the predominating organism in the culture, relapses take place from new infections by a different variety of germs. If autogenous vaccines are to be continued, reculturing and another vaccine is necessary. This complicates matters and often discourages the patient before a cure is effected. Furthermore, the time required to prepare an autogenous vaccine causes such delay that their use is entirely impractical in the early acute stages. Properly selected stock vaccines almost invariably

serve the best purpose. Naturally, in view of the fact that mixed infections predominate, or are liable to take place before a cure is obtained, mixed vaccines should be employed, not with the idea of instituting a hit-or-miss treatment, but for the purpose of establishing a prophylactic immunity towards probable infections while at the same time therapeutic immunization is being developed towards the organisms present in the infection.

In my early experiences with stock vaccines in the treatment of acute colds, I usually depended on clinical symptoms to make a diagnosis for the first inoculation and then verified the diagnosis both from slides and culture growth. Pneumococci and streptococci and more often both organisms were, however, such constant factors that after extensive experience with this method, bacterial examinations to verify the diagnosis were not frequently undertaken, and mixed stock vaccines were used empirically. I fully realize that pneumococci and streptococci are quite generally found in the nose and throat under normal conditions, but this does not negative the pathogenic character of the pneumococci and streptococci that are so constantly and abundantly found in these acute catarrhal infections.

From extensive experience in the treatment of acute "colds" the importance of immunizing against pneumococcus and streptococcus infections has made a profound impression on my mind, because these organisms are liable to cause so many remote serious infections, and even where the infection is primarily due to a Friedlander bacillus, influenza bacillus, or some other organism, pneumococci and streptococci come in as secondary invaders and become the dangerous factor. So, when selecting a stock vaccine for treating colds it is important that pneumococci and streptococci should be the predominating organisms. To be efficient the vaccine should be prepared from a variety of strains among which the most virulent types predominate.

As staphylococci are so constantly present as secondary invaders, with marked pathogenic tendencies where other organisms are involved, and because of the great prevalence of the micrococcus catarrhalis in catarrhs of the respiratory tract, it is a distinct advantage to include these two organisms in a stock vaccine for the routine treatment of colds.

Treatment should be started early, before the infection has become extensive, to obtain the best results. One or two days' delay simply unnecessarily prolongs the disease and increases the danger of complicating extensions of the infection. To avoid unnecessary reactions, the initial dose should not be large. From experience we find that a polyvalent mixed vaccine of about 20,000,000 streptococci, 30,000,000 pneumococci, 100,000,000 micrococcus catarrhalis and 200,000,000 staphylococci, injected subcutaneously, constitutes a good average initial adult dose. Infants or children should be given from one-fourth to one-half this amount. From such a dose, as a rule, nothing more than a moderate amount of inflammation several square inches in area will develop at the site of inoculation. Constitutional reactions, beyond a slight malaise, will seldom take place.

Within 24 hours marked improvement, with a cessation of the acute irritating symptoms, should be observed; but in case marked improvement has not taken place a slightly larger dose should then be given. Within another 24 hours, almost invariably, it will be found that the "cold is broken," with but little indications of the trouble remaining. In cases where marked improvement takes place within the first day it is advisable to repeat the inoculation on the second or third day, and where two doses on successive days were given it is also advisable to give another, somewhat larger dose, two days after the last inoculation. After this two or three more injections should be made at five to seven-day intervals with increasing doses as indicated by the amount of reaction. Where not much reaction is observed

the third or fourth may be three or four times the size of the first inoculation, otherwise the dose should not be so rapidly increased.

Where a cold has been allowed to progress for several days, and especially where the infection has extended to the ear or sinuses, such uniform beneficial results are not obtained, but marked improvement should be looked for within two or three days, with a cessation of pronounced abnormal symptoms within five days or a week. Where vaccines are employed in these acute colds, not infrequently an increased discharge from the nose is observed during the first or second day after the initial dose without producing symptoms of an increased amount of inflammation or distress. This discharge is usually thinner and indicates that a flushing of the inflamed parts with blood serum is taking place. Later on, when the inflammation has almost entirely subsided, we often have the reverse condition. At this time the mucous is often very tenacious, requiring considerable effort to expel it, but is rather scant in amount. This is most noticeable in the morning, after a night's sleep.

An immunity thus established from vaccine inoculation is more lasting than if spontaneous recovery takes place. This is particularly noticeable with individuals who are "subject to taking colds." No one can appreciate the therapeutic and prophylactic efficiency of bacterial vaccines more than a physician who has had occasion to use them on himself and on members of his own family. I was one of the victims of repeated colds. The infection usually started on the posterior part of the palate and simultaneously extended up into the nose, around the pharynx and into the larnyx, and usually, but not always, down the trachea and into the bronchi. I seldom recovered from these attacks in less than four to six weeks, and usually had them about three times a year. During the past eight years, since I have been treating myself with vaccines, no attack has lasted over

two weeks and usually all the symptoms disappear within a few days. Furthermore, I find that these colds are of less frequent occurrence and require less persistent treatment to overcome them than formerly. At first it required six, eight, or a dozen inoculations to hold the infection in subjection and to prevent relapses, whereas now one or two inoculations will suffice. I have noticed the same tendency in other members of my family and the same may be said of patients that have been under my care for a number of years. Other doctors have had the same experience with the use of vaccines. George M. Coates (New York Medical Journal, July 10, 1915, for instance, says:

"The use of vaccines for prophylactic immunization against acute rhinitis, or common acute colds, has come into quite general use and is often very effective. From the number of different organisms causing these attacks, it is manifestly proper and necessary here to use a mixed vaccine, and from the nature of the case it must also be a commercial stock. The duration of immunity, when well established, varies from four months to a year or more, and this treatment is of particular value in that class of cases having a succession of colds lasting throughout the winter, either complicated or not. The organisms most frequently found in these cases are the different varieties of the staphylococci, streptococci, pneumococci, micrococcus catarrhalis, and, when the tendency is to extend to the trachea and bronchi, Friedlander's bacillus. For immunization, then, a commercial mixture of these, made by a reliable firm, is selected, and one-half the regular dose, usually 0.5 c.c., injected. Three days later three-quarters of the dose is given and again in three or four days, the whole dose. I will mention the average doses for the different organisms and the technic of injection at the close of the paper. This should insure the ordinary person against an attack for some months, but in very susceptible individuals the entire course may have to be repeated. To cite my own case, I was immunized during an acute cold twelve months ago, and have not been troubled since, although I was accustomed to have one or two colds a year. Our dispensary clerk at the Pennsylvania Hospital, coming into fre-

quent and close contact with hundreds of people daily in a rather stuffy room, formerly had a succession of colds. Immunization in April kept him free from infection till October, when he was reimmunized and has been well since. Many such instances are available.

"The treatment of an acute rhinitis, once started, is precisely the same as for prophylaxis, except that it is pushed a little more vigorously and continued till the trouble has been conquered. When this has occurred, your patient should be free from danger of subsequent infection for a time. Following the first dose or two, and this is true of all the diseases to be considered, there will most probably be some exacerbation of the patient's condition with increased discharge, which should soon clear up. I do not mean to say that all cases will react favorably, but many will, and the procedure is well worth a trial."

Extracts From General Literature.

Fisher (Boston Medical and Surgical Journal, June 5, 1913), from extensive experience with the use of bacterial vaccines in the treatment of colds, sums up the results thus:

"1. Colds, so-called, are unquestionably due to infection by micro-organisms.

"2. Colds are contagious.

"3. Colds can be largely prevented by reasonable isolation of every case, and preventive inoculation.

"4. Colds can be aborted or their course shortened by vaccine treatment.

"5. The treatment of acute and chronic inflammation of the respiratory tract by vaccines is specific.

"6. A symptom complex resembling influenza may be due to other organisms.

"It is only too true that one swallow does not make a summer, neither do a few cases prove conclusively the value of a new method of treatment. It is, however, my firm conviction that with a properly prepared vaccine, containing the etiological germ, administered with proper dosage and intervals, success will always attend this method of treatment.

"The doctor who off-hand condemns vaccines has either never used them, has not mixed them with brains, has expected them to do the impossible, or he has not had the infecting germ in the vaccine used."

It will be of interest to see what Allen ("Vaccine Therapy," third edition, p. 169) says concerning the importance of immuno-therapy in acute colds and will quote as follows:

"Pneumococcal infections of the respiratory tract assume so many forms, and are so especially dangerous, that I make no apology for emphasizing the following points: In acute attacks the infection usually begins in the larynx or upper part of the trachea, but may begin in the naso-pharynx; the cough is paroxysmal and very distressing, and results in a tiny blob of a very tenacious colorless mucous. The infection spreads simultaneously upwards and downwards, the mucous becomes much more copious, yellow, purulent, and less tenacious, but the distressing cough continues. Pulse and temperature may be little affected. The infection may stop at the bifurcation of the trachea, or it may spread into the bronchi and bronchioles and produce an acute bronchial catarrh. Herein lies the chief danger; after a longer or shorter interval the patient may recover completely without vaccine treatment; but if the bronchial secretion be examined pneumococci will probably be found in abundance. Here they may lurk for weeks or months until climatic conditions or careless exposure to damp or draughts determines the lighting up of the dormant infection. The result of this may be bronchitis of the larger tubes, capillary bronchitis, pneumonia or pleurisy. I have seen each of these sequelae in those treated upon conventional lines, and if I can help it, never allow a sufferer from pneumococcal cold to dispense with vaccine treatment, this being continued if possible until careful examinations of the sputum no longer show the presence of the pneumococci. Such completely satisfactory results are hereby obtained that neglect of a medical man to urge the necessity of vaccine treatment in a case of pneumococcal cold, especially in an aged subject, is little short of criminal."

He advises that treatment be started with a polyvalent stock vaccine "at any stage of the attack—the earlier the better," to be followed up by an autogenous vaccine, and concludes the advantages of treating an acute attack of catarrh upon these lines as follows:

"1. Convalescence is speedier—sometimes almost complete in 24 to 36 hours.

"2. The stage of thick mucous secretion is either practically eliminated or rendered much shorter and less distressing.

"3. The use of expectorant drugs, which so often upset the digestion, may frequently be dispensed with.

"4. The risk of complications is very considerably lessened. Indeed, I venture to say that if this treatment were universally adopted, we should almost cease to hear of deaths due to pneumonia following upon so-called influenza, which in most cases is a pneumococcal cold pure and simple. Heart failure, arthritis, neuritis and the other complications would be equally rare."

Dr. H. M. Starkey (Medical Brief, June, 1911, p. 332) reports some experiences which aptly illustrate the advantages of vaccine therapy in these cases:

"Case 1. Mrs. C. P. Within a year previous to last June had ten severe colds in the head. She came to me June 15th, with a fresh cold well under way. She was given mixed streptococcus pyogenes 30,000,000 and micrococcus catarrhalis 100,000,000, and told that she would probably require another injection in five days. She was receiving treatment for catarrh. The cold was gone in 36 hours, and there has been no recurrence and she has had no subsequent injection and no treatment of any kind for nearly three months.

"Case 2. E. P., age 13, son of the lady just mentioned, has had something like hay fever each summer for several years past. The trouble comes on in June with coryza and bronchitis, and a cough and nervousness that prevent eating and sleeping, so that by Fall the lad has been a physical wreck. The symptoms had been showing their usual severity for three or four weeks, when he came to me about the middle of July. I gave him vigorous local treatment and three-fourths of a dose of streptococcic vaccine, and repeated it in one week. The symptoms were rapidly improved and disappeared within two weeks. He has come through the summer in good condition. Twice he has had some cold and has received injections and the cold has disappeared.

"Case 3. Mrs. S., has been apt to get a cold each Fall that appeared as a sore throat, then next day as a cold in the head, quickly involving the bronchi and causing a cough

lasting from one to two months. The usual cold occurred this Fall about October 1st, and the sore throat of one day had passed into the coryza of the next, when to local treatment was added a dose of mixed streptococcus and micrococcus catarrhalis. In thirty-six hours the cold had disappeared without bronchitis and without cough and there has been no recurrence.

"Case 4. Mrs. W., under treatment for chronic catarrh with middle ear disease and subject to severe attacks of cold in the head, usually lasting several weeks and increasing the ear trouble, came with one of her severe colds of two days' standing October 16th. She had a rather severe sore throat, and the nose was stopped, but the nose and eyes were flowing freely and she was altogether miserable. I gave her beside appropriate local treatment an injection of 30,000,000 of streptococcus pyogenes and 100,000,000 of micrococcus catarrhalis. She went from my office, without my knowledge, to a large unheated room, where she remained giving instructions for an hour or more. She went to bed soon after and was taken with high fever and severe sore throat so that she thought she had caught more cold, and was in for a siege. The symptoms became so severe that before midnight she had to send for a doctor. The symptoms rapidly subsided and by morning she was so much better that she went out for her usual duties, which are very arduous. In a few days the cold had entirely disappeared, much more quickly, she says, than she had ever had one go before, and without bad effects to the hearing or otherwise."

Dr. B. W. Rahney (Journal Indiana State Medical Association, July 15, 1911, p. 303), in referring to the use of vaccines for colds, says:

"Another promising field for vaccine treatment is in acute colds, results in some instances being most surprising, the colds disappearing in 24 hours."

If acute coryzas are prevalent during an influenza bacillus epidemic, or where the Friedlander bacillus is frequently found as the predominating factor, it is necessary to include the influenza bacillus or the Friedlander bacillus respectively in the vaccine employed in the treatment of ordinary colds. To use an influenza bacillus or Friedlander bacillus

vaccine without combining them with the pneumococcus or streptococcus will not give practical results. Pneumococci and streptococci soon become complicating factors as a result of the irritation by the primary invading organism, and unless a simultaneous immunity is developed only a partial relief is obtained.

Treatment should be pursued by making inoculations at about the same intervals as when treating "colds" and the doses should be approximately the same; that is, using the pneumococci and streptococci in the combined vaccine as a guide. The adult dose of the influenza bacillus or Friedlander bacillus should range from 100,000,000 to 300,000,000. Improvement should follow as promptly as where vaccines are employed in ordinary colds. If, in the treatment of colds or these more complicated infections, prompt improvement should not take place with this routine method of treatment, careful bacterial examination should be made of specimens obtained by means of sterile swabs from the nose and throat, to determine what additional organisms may be the cause of the trouble and then prepare an autogenous vaccine from the unusual germ, if found.

This method has been so satisfactory in my hands that I have no hesitation in saying that if it were generally adopted practically all the severe complications following colds, pneumonia, arthritis, mastoiditis, endocarditis, and other ailments, would be eliminated, because in this way the patient becomes immunized against the pathogenic organisms causing the trouble early in the course of the disease while the system is still in a condition to respond readily to the immunizing influence of the vaccine. Furthermore, these colds are disagreeable afflictions even in cases where no serious complications follow and should be cured with the best means at our command.

Any physician who has used these vaccines in colds will soon become a convert to this method, and especially if he

uses them on himself during an attack. In this way he will not only appreciate their therapeutic value but he will also thoroughly realize their harmlessness.

Catarrhs are so liable to become chronic under conventional treatment that the early use of the vaccines becomes an important factor. When the vaccine method is employed in the acute stage these cases are cured before they become chronic. One characteristic feature of the vaccine treatment in sub-acute and chronic infections of the respiratory tract is the marked general improvement that is noticed even before the local infection shows much change.

CHRONIC CATARRHS OF THE NOSE AND THROAT.

Chronic catarrhs are entirely too frequently met with. This is a natural consequence of inefficient treatment with conventional remedies during the acute stages of the infection, and in all probability will be a condition not often met with when immunotherapy comes into general use. In the treatment of these cases a careful examination of the nose and throat should be made to determine the presence of abnormalities or a possible pent-up pus cavity. It is a well-recognized fact that abnormal conditions which obstruct a free movement of the air are always conducive towards penning up infective foci and in such cases it would be unreasonable to expect vaccines to give permanent results without instituting surgical interference. Where deformities exist they should be corrected and pus accumulation should be drained. But when contemplating such operations it is good practice to give a few doses of vaccine so as to build up an immunity and in this way hasten the healing process and avoid postoperative extensions of the infection. The same may be said of adenoids. They should be removed and immunotherapy instituted to hasten recovery. It will be found that where vaccines are employed in conjunction with surgical treatment of the nose and throat

much better results are obtained than where immunization is neglected. But, aside from these surgical cases there is no denying the fact that we frequently meet with cases that are troubled with catarrh in which there is no material physical disturbance, but the individual "catches colds" easily and from frequent attacks becomes a chronic sufferer.

The same micro-organisms are found in chronic catarrhs that are present in the acute infections and for that reason the same combined vaccines are employed. Inoculations should be made at longer intervals and treatment continued over a longer period of time. Where there is much mucous and especially if associated with a bad odor, the Friedlander bacillus is liable to be one of the offenders. A mixed vaccine containing this organism should then be employed. Treatment should be started with the usual small initial dose, because large doses are liable to cause considerable reaction. While this would do no harm, yet it is liable to discourage the patient and create a suspicion that the treatment might be dangerous. By starting with a small dose this is avoided and just as good therapeutic results are obtained. The inoculation should be repeated in about four or five days and the size of the dose gauged by the amount of reaction that developed from the previous injection. If there was no constitutional reaction with slight fever and only a small local infiltration, several square inches in area, at the site of inoculation, the second dose may be increased to one-third more than the previous inoculation, but if there has been more extensive reaction the subsequent dose should not be materially increased. After a few inoculations it will be found that the reactions become less pronounced and after four or five inoculations not much reaction will develop from a full-sized dose.

The question here naturally arises whether the dose should be continually increased to a point where a distinct reaction is obtained, or to continue treatment with the aver-

age large dose. This depends entirely upon how the patient responds to the treatment. Some patients will tolerate crowding, while others will become irritable under too vigorous treatment. I am confident that many users of vaccines have failed in chronic infections because they overtreated their patients, whereas others have failed by insufficient dosage and making inoculations at too long intervals. Here good judgment and close observation of clinical symptoms counts for much. As a rule, however, we can figure that if there are symptoms of slight aggravation in the infected area a day or two after the inoculation the dose has been too large to obtain the best results. In chronic infections, inoculations at from five to seven-day intervals is a good average, and as a rule the average full-sized adult dose is large enough.

Where marked clinical improvement does not take place after a few inoculations a bacterial examination should be made, culturally and microscopically, to determine the presence of unusual organisms, when a corresponding stock vaccine should be given or an autogenous vaccine should be prepared and employed.

In the more obstinate cases treatment must be persistently followed up for four to six months or more, to get permanent results, and even in these cases relapses are liable to take place when acute colds are encountered, but gradually the condition will be brought under control. Local cleansing with normal salt solution or by employing mild antiseptics is an important adjunct to the vaccine treatment and should not be neglected.

ANTRUM AND SINUS INFECTIONS.

Antrum and sinus infections are due to extensions from acute nasal catarrhs and naturally the same micro-organisms are found that prevail in the so-called colds. The primary invaders usually correspond to the type of organism

prevalent at the time when the acute coryza exists, but later in the course of the infection the more persistently pathogenic organisms may supplant the original invaders entirely. There is good reason to believe that sinus infections take place more frequently than is usually suspected, spontaneous recovery taking place in most instances. It is also probable that antrum infections take place much more frequently from acute nasal catarrhs than from infected teeth.

From the fact that sinus infections, when once established, have a tendency to become chronic, it is of utmost importance to institute immunotherapy early and by this means effect a cure before infective infiltrations and inflammatory deposits have time to develop a chronic condition.

While instituting vaccine treatment in sinus infections it is necessary to make a careful examination to determine abnormalities which require surgical corrections. Proper drainage should be established and where antrum infections are due to infected tooth-sockets the teeth should be taken care of.

The most constantly pathogenic organisms in sinus infections are the streptococcus, pneumococcus and staphylococcus. The micrococcus catarrhalis and Friedlander bacillus are also often found. During influenza bacillus epidemics this organism predominates. The bacillus pyocyaneus, colon bacillus, and pseudo-diphtheria bacillus are occasionally found. Mixed infections are common and for this reason it is always advisable to employ a mixed vaccine containing the usual organisms found in these cases. In the acute cases inoculations should be made at daily intervals, and after the more acute symptoms subside, from four to six days apart. In subacute and chronic conditions vaccines should be given the same as in chronic catarrhs.

The experiences of Ross Hall Skillern (The Laryngoscope, July, 1914) aptly illustrate the advantages of early vaccine treatment in sinus cases:

"Previous Experiences: Several years ago I used autogenous vaccines on a small number of cases of chronic purulent ethmoiditis and while the immediate results appeared to show improvement the ultimate results were not sufficiently encouraging to warrant continuing their use.

"Present Experiences: Within the past few months we have instituted treatment of sinus suppuration with stock vaccines. The number of cases treated were twenty—frontal acute 3, chronic 4; ethmoidal chronic 8; maxillary acute 3, chronic 2. Injections varied from two to twelve. The quantity began at ½ c. c. and at fourth injection 1 c. c. No. 36 Sherman was invariably used. Formula: Friedlander bacillus 300,000,000, micrococcus catarrhalis 200,000,000, streptococcus 60,000,000, pneumococcus 80,000,000, staphylococcus aureus and albus a. a. 200,000,000. In the acute cases two or three injections sufficed, while the chronic cases always went to the full number.

"Results Immediate: The results within two days were often so good as to delude one with false hopes. The local reaction where the injection was made was always marked from the first application, appearing as a greater or lesser soreness and stiffness in that portion of the arm or leg. Subsequent injections provoked this reaction less and less. The sinus condition was usually better although in the chronic cases the discharge was often worse and occasionally unaffected. The two or three subsequent injections seemed to bring continual improvement, and while this was real in the acute cases, in the chronic it was ofttimes but apparent. Up to the present none of the chronic cases have been absolutely cured although many show great improvement.

"End Results: Frontal sinus, acute 3, chronic 4, cured 3, benefited 2, not improved 2. Maxillary sinus, acute 3, chronic 2, cured 2, benefited (acute) 1, (chronic) 2. Ethmoid cells, chronic 8, cured 1, benefited 3, not improved 4. Total cured 6, benefited 8, not improved 6. Percentage of cures in acute, 5 of 6, or 86 per cent. Percentage of absolute failures in chronic, 6 of 20, or 30 per cent.

"Conclusions: 1. This therapy is of great value in acute cases which are slow in healing and tend to become chronic. 2. It should be a routine procedure in all chronic conditions which show a tendency to be of the latent type. 3. It should

be administered after radical operations. 4. It offers the most hope in old operated cases which have not been entirely cured or have become reinfected."

Dr. Clifton M. Miller (Charlotte Medical Journal, December, 1914) gives a detailed report of sinusitis treated in most instances with a mixed stock vaccine with uniform beneficial results. In defense of the use of stock vaccines he says:

"These cases, except where noted in the case reports, were treated with mixed stock vaccines containing staphylococcus albus, streptococcus, diphtheroid bacilli, diplococcus pneumoniae and micrococcus catarrhalis.

"The use of combined stock vaccines has been attacked as being unscientific and hence unjustifiable, but it seemed to me, particularly in nasal affections, that the great variety of the bacteriological flora of the nose justified their use when conditions of investigation or the patient's circumstance made it impracticable to use autogenous vaccines.

"The use of stock vaccines and their failure in a given case does not indicate that this case may not be cured by autogenous vaccines nor can we mark it as a therapeutic failure of vaccine therapy until a carefully prepared autogenous vaccine has been used."

Where improvement from a mixed stock vaccine does not take place soon after instituting treatment, careful cultural and microscopic examinations should be made to determine the presence of unusual organisms, and if found, a corresponding stock vaccine or an autogenous vaccine should be employed.

Infections of the upper respiratory tract sometimes develop queer complications by unusual extensions of the infection. The following case will serve as an illustration: Some years ago a man aged 28, married, called at my office and complained of intolerable pains in the head. There was no history of syphilis or gonorrheal infection. About six months previous to this time he had had an acute rhinitis which had not entirely cleared up, and soon after the cold started a pain developed back in the head between the eyes,

which steadily grew worse. The pain, while continuous, usually got worse about noon and continued till after midnight, when he would get three or four hours' sleep with some relief mornings. During the time when the pain was most severe hot applications over the forehead and eyes with the head well elevated, while lying down, gave some relief. His vision was impaired. With the left eye only large type could be seen. The right eye was not so bad, but ordinary type could not be distinguished. Examination with the ophthalmoscope revealed nothing abnormal in the eyes. Prior to this illness his vision had been normal, he never having worn glasses; examination of the nasal cavity revealed a slight catarrhal state with most of the inflammatory condition high up in the nose. There was no fever nor had there been any that attracted attention. He had been under the care of the family physician for three months and for six weeks had been treated by a competent oculist. He told me that the doctor had considered his trouble due to a tumor developing at the base of the brain and was causing pressure on the optic nerves. That was a plausible explanation for the symptoms, but by associating the fact that the illness started with a coryza which had not cleared up it occurred to me that there was a possible connection between the nasal infection and the then existing condition. Knowing the streptococcus to be a common invader of the upper respiratory tract and that this organism often causes chronic infections without pus formation, I concluded that vaccines might do some good and could do no possible harm. So vaccine treatment was started by giving a dose of combined vaccine containing 30,000,000 streptococcus and 100,000,000 each of staphylococcus aureus and albus, with the result that much relief from pain was observed within two days. Four days later the same vaccine was repeated, and the dose gradually increased to double this amount, making inoculations at weekly intervals. The case progressed rapidly and in two months' time was entirely well, with normal vision and relief from pain.

Two years later I was called to see him again. At this time he was confined to bed with an attack of measles. The expectant plan of treatment was followed and recovery took place in the usual length of time. About four weeks after convalescence he called at my office complaining of the same pain back of his eyes, with impaired vision. Two doses of the same vaccine was all that was necessary to clear this up entirely. I heard nothing more from this patient until several years later when his father called at my office and informed me that he had gone west, I think Oklahoma, where he contracted typhoid fever and died.

TONSILLITIS.

Infections of the tonsils are common, both acute and chronic. Here the streptococcus is the most common invader. Usually the less virulent types of this micro-organism are present, but the more virulent types are also frequently found. In making a clinical diagnosis of tonsillitis the fact that membranous exudate resembling diphtheria is often found to be due to streptococci should never lead one to neglect giving diphtheria antitoxin at once where a reasonable suspicion exists that the case may be one of diphtheritic infection and the diagnosis verified by bacterial examination. If the symptoms indicate severe infection a vaccine should be given in conjunction with the antidiphtheric serum, because by this means active immunization will be hastened towards streptococcus involvement while the antitoxin is establishing a passive immunity towards a possible diphtheria infection. By this method the patient is safeguarded against both diphtheria and streptococcus infection without possible harm from either direction. Furthermore, complicating infections by the streptococcus in diphtheria are not uncommon and by using streptococcus vaccine in conjunction with the diphtheria antitoxin a definite purpose is served. I am confident that in many cases of diphtheria where the inflammatory condi-

tions do not subside promptly after giving antidiphtheritic serum, secondary streptococcus infection is an important factor which may be relieved by employing vaccines in conjunction with the serum.

While most cases of tonsillitis are due to the streptococcus, yet in some cases the pneumococcus is found and the staphylococcus is commonly an associate, probably a secondary invader. The micrococcus catarrhalis is so often found in crypts of inflamed tonsils that this organism may also be considered a pathogenic factor. Tubercular infection of the tonsils will be considered under tuberculosis.

From the bacterial flora of tonsillitis it is clear that the same combined vaccine usually employed in treating acute colds also applies here. The initial dose should be about 20,000,000 streptococci, 30,000,000 pneumococci, 100,000,000 micrococci catarrhalis, and 200,000,000 staphylococci. In acute cases treatment should be started early and a slightly larger dose given the next day. When treatment is started before a necrotic center has developed, abscess formation can be avoided. Usually marked improvement is found by the next day and within two or three days the acute inflammatory condition is entirely relieved. Where treatment is started later, much of the inflammatory infiltration and pain is relieved, but will not clear up if abscess formation has begun until drainage is established, after which recovery is very prompt.

The importance of applying immuno-therapy in acute tonsillar affections can not be overestimated when we consider the serious complications which often follow if the infecting organisms gain entrance to the blood current from the inflamed tonsil and become localized in remote parts of the body, as in endocarditis or arthritis. The streptococcus responsible for these systemic infections evidently possess poor antigenic properties for antibody production. It offers enough resistance to destruction to

remain an active infecting agent for weeks or months, while circulating in the blood or localized in the tissues, if the patient survives.

Dr. John A. Oille, of Toronto, Ontario (Journal A. M. A., Oct. 2, 1915, p. 1160), cites a striking series of tonsil infections followed by other complications as follows:

"In another family the spread of tonsillitis and associated diseases was remarkable. The mother, who has often had nervous breakdowns, had tonsillitis in December. Shortly afterwards the husband had it also, followed in a month by appendicitis, and two or three weeks later by a second attack with operation. While he was in the hospital the daughter, aged 5, had tonsillitis, after which slight fever persisted for five or six weeks and a pulmonary and mitral systolic murmur developed for the first time. During this interval the baby had a sore throat. About the same time the nurse went home with tonsillitis. While she was away the other maid, the last member of the family, was taken ill with appendicitis also, with operation. While the little girl was ill with endocarditis the mother's sister came on a visit and two or three days after her arrival she too had an attack of tonsillitis. Several other members of the mother's family have had tonsillitis often, some with endocarditis."

By employing polyvalent vaccines during the primary tonsillar infection the superior antigenetic properties of the killed organisms will stimulate sufficient antibody production to build up a systemic immunity and prevent systemic invasion of the bacteria. It may be argued that the streptococcus viridans is the most common variety of the streptococci that cause tonsillar infections followed by blood invasion and heart or joint infections, and that autogenous vaccines prepared from this organism, when isolated from the patient's blood, do not give encouraging results. In this connection it should be realized that vaccine treatment has usually been neglected in these cases until cardiac involvement has occurred to a point where permanent damage has been done to heart valves, so that death will ensue from a leaky heart that is beyond repair. Experience also

shows that in cases of infections of long standing a certain tolerance to the infecting organism is developed and that vaccines prepared from such organisms are often not adequate therapeutic agents when used on the patient from which the organism was acquired. Furthermore, as pointed out in the chapter "'Autogenous or Stock Vaccines," clinical experience shows that there is a certain group action in the immunizing response; that there exists a certain overlapping in the immunizing properties of the various strains or types of organisms, and that to a polyvalent vaccine which contains various strains of organisms, the immunizing faculties respond more promptly than to a single strain to which a certain tolerance has already been established. When polyvalent stock vaccines are given during the acute tonsillar infection the immunizing faculty is still in a condition to respond promptly to vaccine inoculation and consequently avoid systemic invasion.

In cases of chronic tonsillitis, temporary good results may be obtained by vaccine inoculations, but the condition is liable to relapse. Many people are susceptible to tonsillar infection and have repeated acute attacks. In these repeating acute and chronic cases, where an active infection of a tonsil exists, vaccine treatment should be instituted until the acute inflammatory condition subsides, and then the tonsil should be enucleated to avoid further trouble.

ATROPHIC RHINITIS.

In 1899—1901—Perez, of Buenos Aires, reported that he had succeeded in isolating the organism causing ozena, and described it as the coccabacillus foetidus ozena Perez. Subsequently Perez was sent to Austria as ambassador of Argentine, and induced Viennese rhinologists to undertake experimento-clinical researches along the lines of his work.

Hofer (Wiener klin. Wochenschrift, 1913, No. 25) agreed with Perez's conclusions: He found the coccabacillus in the

nasal secretion of the majority of cases of genuine ozena; it produced in rabbits a perfectly analogous pathological condition, developed on artificial culture media the typical ozenic fetor, and was agglutinated by the serum of ozena patients in part of the cases. Later (idem, 1913, No. 42) Hofer reported a series of cases treated in the clinics of Paltauf and Chiari with a polyvalent stock vaccine prepared from seven different strains. After eight weeks' experience he found that it produced lessening of the secretion, crust formation and fetor; cure of introitic eczema; retrogression of posterior swelling; improvement and even cure of dry pharyngitis in all cases; and improvement of phonation in one case with dry laryngitis.

Mazza (Wiener klin. Wochenschr., May 6, 1915) employed at first a vaccine made from three strains of these organisms, but later he used one made from six strains—in doses of 500 millions—and obtained correspondingly better results. The first changes noted were active congestion of the inferior turbinates associated with small extravasations of blood, occasionally epistaxis. The day following the injection the white parchment-like spots observed in this disease disappeared and vascularization occurred. Secretion became thinner and more abundant, and patients who had not been able to blow the nose because of the thick crusts found no difficulty in so doing after the injection. The second dose was given after a weeks' interval, and the benefit was even more apparent.

Dr. H. Horn, of San Francisco (Journal of the American Medical Association, Aug. 28, 1915) reports some extensive experimental work with cultures of the Perez bacillus obtained from Hofer, of Vienna. While typical lesions were obtained in inoculated rabbits aggulutination tests were negative.

Concerning the use of vaccines in the treatment of ozena he says:

"This, then, brings us to the most important part of the the subject, namely, the treatment. One fact stands out without question, and has been proved so often that it needs no support. Cases which clinically would be classed as true ozena have been vastly improved temporarily and possibly permanently by the administration of several of the stock vaccines on the market, which usually contain the Friedlander baccillus. Micrococcus catarrhalis, pneumococcus and streptococcus.

"This may raise two points: 1. Is ozena possibly a mixed infection? 2. Are there certain types which cannot be clinically differentiated and of which the Perez bacillus is not the etiologic factor? It would also seem possible that some of our many failures are due to the fact that the growth of the various extraneous organisms in the nose are for the moment more important than the Perez bacillus and that perhaps our results would be better if we preceded the treatment by the use of a stock mixed vaccine, to be followed in turn by a vaccine made from the Perez organism or possibly, as we are now considering a combination of the Friedlander bacillus, Micrococcus catarrhalis, pneumococcus and streptococcus, with a vaccine made from the mixed strains of the Perez bacillus."

His case reports show quite conclusively that beneficial results were obtained from the Perez bacillus vaccine prepared from the strains obtained from Hofer.

In a supplement which I received with a reprint of his paper he states that he succeded in obtaining serum from rabbits immunized according to Hofer's method which agglutinates with clinical cases of ozena. He also states that he succeeded in isolating the organism from cases of ozena and is using a vaccine prepared from six strains with better results than was obtained from the European strains.

Drs. Murray and Larson of Minneapolis (The Laryngoscope, November, 1915) report some experimental and clinical work which they did with the Perez bacillus. The results of their work was not encouraging however, as shown by their summary and conclusions as follows:

"Summary (Experimental). In experimental work, 27

rabbits were injected with cultures of Perez baccilli received from Hofer. We were unable to confirm the work of Perez and Hofer in which they state that their bacillus shows a selected affinity for the nasal mucosa. We did succeed in isolating the organism from the nasal passages of four rabbits but it must be emphasized that we never succeeded in isolating the organism from the nose save in those cases in which it was also present in the heart's blood. In none of the 27 animals used in our experiments was there any evidence of atrophy of the turbinate bodies. 24 ozena patients were examined bacteriologically, according to the method recommended by the Vienna author; all gave negative results. Agglutination tests were made from the blood of 34 ozena patients but no frank agglutination reactions were recorded. The complement fixation reactions were likewise negative in the six cases examined.

"(Clinical) Age of onset: 12, (3), 10, 20, 5, 29, 6 (12), 17, 19, Constitutional diseases: Wassermann, negative in all cases. Evidence of tuberculosis: absent in 11 out of 12 cases. Inferior turbinates: atrophy in all cases. Middle turbinates: some degree of atrophy in 5 cases. Hypertrophy in 4 cases; normal in 8 cases. Pharynx: atrophic pharyngitis in 10 cases. Follicular pharyngitis in 2 cases. Similar nasal affection in family: in Case 5, father had atrophic rhinitis; in Case 8, one sister had atrophic rhinitis; in Case 10, mother and brother had atrophic rhinitis. In seven of the cases there was no family history of similar nasal condition. Contact with animals: Cases 5, and 10 gave history of having come into contact with dogs prior to and at onset of nasal affection. Reaction following injection of vaccines: some local reaction, at site of injection, occurred in Cases 1, 2, 5, 7, 8, 10. Increased nasal discharge followed injection in Cases 3, 6, and 8. Headache and slight malaise followed injection in Cases 3, 6, and 8. Results: some degree of improvement, subjectively or objectively, in Cases 2, 5, 6, 7, 8, and 12. No improvement in Cases 1, 3, 4, 9, 10, and 11. Crust formation: there was objective improvement in size and quantity of crusts in cases 2 and 12. No change in crust formation could be noted by examiner in Cases 1, 3, 4, 5, 6, 7, 8, 10 and 11. In Case 2, there was a very noticeale improvement in crust formation, the crusts becoming much smaller in size and loosely attached. Case

12 showed some improvement in size of crusts but not in disappearance of crusting foetor: There was a disappearance of foeter in Cases 2 and 12. Improvement in cases 5 and 8. No improvement in Cases 1, 3, 4, 7, 9, 10 and 11. In Case 6 there was no foetor present at beginning of treatment. Pharyngitis Sicca: pharyngitis sicca was present in Cases 1, 2, 3, 4, 5, 6, 7, 8, 10 and 11. Follicular pharyngitis in Cases 9 and 12. Of the 10 cases of atrophic pharyngitis, dryness and discomfort was complained of in Cases 2, 3, 4, 5, 6, 7, and 10. Subjective improvement followed treatment in Cases 2, 5, 6, and 7. No improvement in Cases 3, 4 and 10."

"Conclusions: Experimentally, our work has been rather disappointing, not having been able to obtain any evidence that the bacillus as described by Perez is the cause of ozena, and we are unable to confirm the experimental work of Hofer.

Clinically improvement was obtained subjectively and objectively in a proportion of the cases reported. There was undoubted objective improvement in crust formation in two cases. There was subjective improvement in foetor and pharyngitis sicca in a larger proportion of cases. A sufficient length of time has not elapsed since cessation of treatment to enable us to state that the improvement obtained is permanent, and it cannot be considered that a cure was effected in any cases. While clinical results have been encouraging in some of our cases, we do not believe that our clinical evidence is sufficient to warrant the belief that the Perez bacillus is the true cause of ozena, and a review of the literature, with a comparison of our clinical results, will show that equally good results have been obtained by other investigators who have used other forms of vaccines in the treatment of ozena."

The probability is that the organism described by Perez is not a new entity, but belongs to the Friedlander group. The value of bacteriotherapy in ozena has been commented on by a large number of American workers. Mosher and Kerr (Boston Medical and Surgical Journal, May 20, 1909) reported ten cases benefited by the administration of combined stock vaccines; the most annoying symptoms—odor, large crusts, dryness of the throat, headache—were im-

proved in all of the cases, and in many of them cured; and their results fully justify the vaccine treatment. Cobb and Nagel (Annals of Otology, June, 1912) narrated six cases of atrophic rhinitis and conclude that vaccine injections, if carried out regularly, produce permanent improvement. Irregular or too few injections cannot be counted on with the same certainty, but marked improvement seems to have followed even in these cases. Fielding and Lewis (The Laryngoscope, July, 1914) refer to a series of atrophic rhinites treated at the Jefferson Hospital Clinic in Philadelphia. Out of seven well-marked cases six were very much improved and one slightly so.

In view of the recognized impotency of conventional treatment in ozena, the use of a combined vaccine (B. Friedlander, 300 millions; M. catarrhalis, 200 millions; pneumococci, 80 millions; staphylococci albus and aureus, aa 200 millions) is certainly well worth while. The dose should be from 0.2 cc to 1.0 cc., gradually raised at intervals of four days to a week. Other indicated measures should not be neglected.

Vaccines in Hay Fever.

That hay fever is the result of pollen irritation is now well established. Why pollen should irritate some people while others are not influenced by it is not so easily explained. The protein sensitization theory is the one that is receiving the most attention at the present time. According to this theory, hay fever subjects have developed the faculty of decomposing or splitting up the protein constituent of pollen, converting it into its toxic and non-toxic radicals similar to what takes place in the production of an anaphylaxis from the injection of horse serum or some other abnormal protein, the essential difference being that in hay fever the process is localized on the mucous membrane where the pollen lodges from the surrounding atmosphere. In other words, hay fever would be designated

as a localized anaphylaxis due to a decomposition of pollen proteins by one who has become sensitized to them.

Pollen vaccines have been employed for the purpose of immunizing the patient so as to create a tolerance to pollen proteins, but so far no great success has been obtained. In this connection the essential difference between immunizing against living pathogenic bacteria and an organic substance like pollen should be taken carefully into account. Immunization to pathogenic bacteria creates a condition which causes the disintegration or destruction of the invading bacteria and prevents their further growth and development, whereas hay fever cases have developed the faculty of destroying the invading pollen, but fresh pollen is continuously being supplied while it is prevalent in the air and it is this continuous process of disintegrating pollen protein with the liberating of the toxic radical that keeps up the continuous irritation. The question here naturally arises as to whether hay fever is really due to pollen sensitization or to the patient's becoming sensitive to pollen. Pollen sensitization would be a condition such as described above where disintegration of the pollen causes the irritation, but it may be that normal resistance to the toxins produced from pollen proteins is sufficient to prevent localized irritation and that only in cases where this resistance is not sufficient, hay fever symptoms will develop. This would constitute a condition of sensitiveness to pollen irritation. If hay fever is a real pollen sensitization, not much if any relief should be expected from pollen inoculations because these inoculations would have a tendency to intensify the existing sensitization; on the contrary, should these hay fever cases merely be sensitive to pollen irritation, pollen inoculations should be of benefit because by this means a tolerance to pollen would be built up.

The fact that hay fever cases show no signs of improvement until the pollen season is over, indicates that no im-

munizing resistance develops during an attack and that the real condition is pollen sensitization.

That pollen irritation is not responsible for all the symptoms present in hay fever can no longer be questioned. We know that pathogenic bacteria are always liable to invade accessible tissues where normal resistance has been lowered by irritants. Pneumococci, streptococci, staphylococci and other organisms are found on the mucous membrane of the nose and throat of most normal individuals and in hay fever cases these organisms are found in abundance. That these organisms are important complicating factors and are responsible for much of the irritation and most of the fever is quite apparent.

Here the immunizing influence of bacterial vaccines is of real value in the treatment of hay fever. By this means sufficient resistance to these pyogenic organisms is developed to prevent them from becoming infective agents following the pollen irritation. The result is that the patient either goes on to complete recovery or the disease runs a modified course, the pollen irritation being the only factor left, which causes comparatively little distress.

From the available records it appears that I was the first to use bacterial vaccines in the treatment of hay fever, on the theory that pyogenic organisms will aggravate the irritation of mucus membranes due to pollen or any other cause.

It is only a few years that bacterins are employed in the treatment of hay fever, but the method has proven so satisfactory that many physicians are using them as a routine in their cases. In my own practice I must say that no other method has proven so effectual. A number of patients who came for treatment had been obliged for many seasons to regularly seek relief by going north, but in no case was a change of climate necessary after vaccine inoculations. In a majority of cases the symptoms were relieved entirely

within two or three weeks, while in others the irritated condition of the mucus membrane continued in a modified form. One striking change was observed by all of them: that they could sleep at night and feel rested in the morning. This of itself is of great advantage.

I find that the mixed vaccines usually employed in the treatment of "colds" generally serve every purpose, but treatment of hay fever should be started with somewhat larger doses at shorter intervals. In my experience a mixed stock vaccine containing streptococcus 60,000,000, pneumococcus 80,000,000, staphylococcus aureus and albus each 200,000,000 and micrococcus catarrhalis 200,000,000 per c.c. has been most extensively exployed. It is advisable to start treatment about a week or two before the usual onset of the disease. This as a rule, however, does not prevent symptoms of hay fever from developing. In some cases the disease will start in with just as much violence as if no vaccine had been given, but it dies out soon. I have seen cases in which the severe coryza lasted but two or three days. The dose is usually 0.5 c.c. and at three- or four-day intervals, gradually increased to 1 c.c. Should bacterial examination show organisms not contained in the vaccine, a corresponding stock vaccine should be employed or an autogenous vaccine prepared. Treatment should be continued for at least two or three weeks at weekly intervals to avoid a relapse and where the case does not clear up entirely vaccines should be employed until the hay fever season is over.

There has not been as much written on the use of bacterial vaccines in the treatment of hay fever as the advantages of this method would warrant, but enough has been said to show that they are being extensively employed. Professor Charles B. Morrey, of the Ohio State University (Journal A. M. A., Nov. 15, 1913), reports eight cases of hay fever treated with autogenous vaccines prepared from micro-organisms found in the nasal secretions with uniform good results. In conclusion he says:

"The cases are few, but are certainly interesting, especially Cases 3, 4, 5 and 7, in which patients were under my personal observation in 1912, as were the patients in Cases 1 and 2 in 1911. The satisfying results of these two led to the continuation of the work in 1912, and the experimental vaccination was an excellent guide to procedure. It appears of promise, also, that these two were much better in 1912, though they took no treatment.

"I have made no attempt to discover any "specific germ" of hay-fever and do not believe that it exists. The theory on which the work was based was the strengthening of the nasal mucosa, so that the irritants, whatever they are, would be without effect."

Dr. J. E. Clark, of Detroit, (Bacterial Therapist, May, 1913, p. 51) says that he obtained very satisfactory results with vaccines in hay fever; three cases being entirely relieved and others much modified.

Dr. Dana Carter, of Thermopolis, Wyo., says that "I have gotten some of the most gratifying results that I have ever seen, with vaccines in hay fever cases—patients who had suffered for years."

Dr. A. G. Huegli, of Detroit, informs me that he uses vaccines regularly in his cases of hay fever with good results.

Dr. A. T. Sherman reports that he has treated 49 patients troubled with hay fever with but three cases that were not materially benefited. Most of the cases treated were recommended by persons who formerly had received vaccine treatment.

A Dutch physician, Kooijman, reports in the Nederl. Tijdschr. v. Geneeskunde, (Aug. 28, 1915), the successful use of a mixed bacterial vaccine in the treatment of severe hay fever. While this writer's report concerns only two cases, it is clear that he is thoroughly convinced of the efficacy of this method of treatment.

Farrington (The Laryngoscope, January, 1914) prepared autogenous vaccine from cultures procured from the middle

turbinates in hay fever cases. An average dose of 200,000,000 organisms was given at four-day intervals. Twenty-five patients were treated, thirteen were cured, six markedly improved, three slightly benefited, and there were three failures. Of the thirteen cured cases, eight were complicated with asthma and of the six markedly improved, five had asthma.

Dr. Kreuscher, of Dr. Murphy's staff, (Surgical Clinics of John B. Murphy, August, 1913) in referring to his experience with vaccines in hay fever, says: "Last August we treated three cases of hay-fever with a mixed stock vaccine containing for the most part the streptococcus. Two of these cases did not find it necessary to change climate during the hay-fever season, as had been their custom for many years."

Drs. Solomon Strouse and Ira Frank, of Chicago, (Journal A. M. A., March 4, 1916, p. 712) treated some cases of hay-fever with pollen and other cases with vaccine to determine which gave the best results. Concerning the results obtained they say:

"In the early part of this summer hay-fever was very light, and for that reason we felt unable to estimate just what were our results. The general impression of most of the patients was that, compared to patients not receiving pollen, they were having comparatively milder symptoms.

"During a hot spell in September, three of the patients, who up to then had been free from symptoms, had most severe attacks of hay-fever. Autogenous vaccines were immediately made and intensively injected. In these three patients, and a fourth in whom vaccine therapy in a previous year had been beneficial, most surprising results were obtained. The three patients who had been having most intense attacks of hay-fever showed after the first injection an almost complete disappearance of symptoms. The fourth patient, who was having only mild attacks at the time, also reacted with a disappearance of symptoms. In all four the vaccines were continued until the end of the season, and in all the results were almost unbelievable and

can hardly be called other than seasonable cures, as the patients had no subsequent attacks. While these results might have been due to the previous inoculations of pollen extract, comparison with the other patients renders this interpretation improbable. Three of these patients had received autogenous vaccines in previous years with some amelioration of symptoms.

"As stated in the beginning, interpretation of therapeutic experiments is extremely difficult. In our tables not a case was thrown out for any reason. Perhaps the most conservative way of comparing results is in figures; 64 per cent of the patients receiving vaccines and 70 per cent of those receiving pollen extract apparently had a milder season than previously. Vaccine therapy seemed to give equal or better results than pollen extract in the individual cases. The past year was an unusually favorable one for hay-fever subjects, but in no case was there a cure from the pollen extract. Whether the amelioration of symptoms either year was due to the therapy cannot be determined. The four patients receiving combined treatment is entirely too few to permit of any definite conclusions. The theory on which combined specific therapy is based seems tenable, and the results so far obtained seem to support the theory; although it is of course possible that, in the light of newer interpretations of certain so-called specific reactions, some other explanation of our results may subsequently be offered. Whether the method of prophylactic pollen therapy combined with phylactic vaccines is the proper one cannot be judged as yet. The question is open and can be decided only by a larger experience than that reported here."

Virgil Dabney (N. Y. Medical Journal, Feb. 10, 1912) summarizes the experiences of McDonald, Weston and Kolmer, Patterson et al, Conners, Mosher and Kerr, Fisher, Jacobs, Thomas, Hoobler, Hones, Scott, Grandby and Sill, together with his own, in the treatment of nose, throat and ear infections with vaccines and gives the following interesting table:

	Number	Cured	Improved	Unchanged
Subacute otitis media	265	186	35	17
Chronic " "	57	13	21	23
Acute maxillary sinusitis	6	6	..	..
" frontal "	0	..	..	..
Chronic " "	8	0	3	5
" maxillary "	17	9	8	..
" ethomoditis "	3	1	1	1
Mastoditis, sinusitis	11	6	4	1
" acute	1	0	1	..
Atrophic rhinitis	13	0	13	..
Coryza	6	1	5	..
Hay Fever	1	1	..	..

CHAPTER VIII.

INFECTIONS OF THE MOUTH AND TEETH.

Infections of the mouth are common and cause a great deal of annoyance and suffering. These infections vary from a slight superficial ulcer to an extensive alveolar abscess or a chronic pyorrhea.

Slight superficial ulcers of the mouth or aphthae are the result of superficial infections by the usual infecting organisms found in nose and throat infections—streptococci, pneumococci, staphylococci. They are liable to develop where the mucous membrane has been lacerated or scratched by contact with teeth, by applying a tooth brush injudiciously, or by other means. When acute infections of the throat exist, very slight injury to the mucous membrane of the mouth will suffice to start one of these ulcers and from the frequency that this condition is met with during acute colds I am inclined to think that these localized infections sometimes take place without the necessity of a previous injury to the mucous membrane.

In adults these mouth ulcers usually heal spontaneously, especially when local treatment of an antiseptic nature is applied, but in infants I have seen cases where practically the entire mouth was involved with a tendency towards a prolonged ailment. The use of vaccines is of distinct advantage in all these cases. In the less severe cases it will be found that the ulcers heal more rapidly than where no vaccine is used and the development of new ulcers which so commonly takes place will be avoided. In severe cases local treatment is often entirely inadequate. Here is where bacterins are of great benefit. Improvement usually soon takes place after the first inoculation. Some people are subject to thrush, and while the ulcers usually heal rapidly,

new ones appear at short intervals. In these cases vaccines are also of great value in that approximate permanent results may be obtained. A combined stock vaccine containing streptococci, pneumococci and staphylococci usually serves every purpose. Treatment should be started with the usual small initial dose and gradually increasing as indicated by the progress made. Ordinarily two or three inoculations at three to five-day intervals is sufficient.

Among the acute infections of the mouth, abscess formations at the root of the teeth, known as septic apical and mandibular abscesses, are the most troublesome to handle and often lead to the loss of teeth that can be saved by the timely use of bacterins and at the same time relieve much pain. Every physician and dentist sees these cases and where no vaccines are employed they generally run a course of several weeks before the inflammatory process is brought under control, and meantime the patient is subject to intense suffering.

An abscess at the apex of the root of a tooth is always a small affair, in fact, so small that the small amount of pus it generates is absorbed without difficulty if the inflammatory process is relieved through immunization. Necessarily, the earlier in the course of abscess formation immunization is established the better are the chances to avoid permanent injury to the tooth and make its removal necessary. The early symptoms of apical abscess formation are deep-seated pain in the tooth with a feeling that the tooth is too long and very painful when biting. As the infection develops, much swelling of the gum and surrounding tissue, with contiguous lymphatic gland involvment, takes place.

Streptococci, pneumococci and staphylococci are, with few exceptions, the responsible infective agents, and from my experience a combined vaccine containing these organisms is of inestimable value in the treatment of these cases. It is good practice to employ vaccines in all cases of toothache while the dentist is taking care of the defective tooth.

Gumboils should be lanced and where fistulous openings exist, necrotic bone should be looked for and removed. Under the immunizing influence of vaccines these cases heal much more rapidly than otherwise.

Medalia (Boston Medical and Surgical Journal, Nov. 27, 1913) reports fourteen cases in which vaccines were used and a few typical cases from the ones he reported clearly illustrate the benefits of bacterins in these cases:

"Case 4. Feb. 28, 1910. F. N. A., female, 28 years old.

"Complained of infected right lower wisdom tooth. 'Tooth itself perfectly sound.' Whole right side of throat and tonsil much swollen. Considerable pain of lower jaw with tightness and rigidity of muscles. Could not open her mouth. Could not masticate. Had to take liquid food. Hurt to swallow. Felt bad generally.

"Examination showed swelling of right submaxillary triangle, extending to right side of throat, tonsil and submaxillary gland. Swollen and tender on pressure. Tongue very much coated and considerable white mucous covering the gum round the lower right molars and throat. No pus.

"Treatment.—Vaccine was administered, 250,000,000 staphylococcus aureus and 50,000,000 pneumococcus.

"March 1, swelling practically gone. Could open her mouth well. Very little pain. Feeling fine generally. Was given another injection of vaccine in the same dose as that of the first day and discharged. She needed no further treatment.

"This case, too, is a good illustration of the possibility to abort an acute abscess by means of vaccine during the hyperemic stage of the disease. Two treatments at an interval of 36 hours were apparently sufficient to check the further progress of the septic process in this case.

"The following (Cases 6, 7 and 8) are some more of the mandibular third molar abscess cases and are self-explanatory. They are similar to those already described:

"Case 6. June 1, 1911. S. W. A., male, 24 years old.

"Complained of a sore wisdom tooth and acute tonsillitis. Had difficulty in swallowing. Caught cold in head and chest. Raised some. Could not sleep the night before because of the pain in tooth. Could take only liquid nourishment.

"Examination showed marked inflammation of the throat. Swelling of left tonsil and submaxillary triangle. Very tender to touch. No fluctuation. No discharge of pus seen. The acute alveolar osteomyelitic abscess in this case was apparently in the hyperemic stage. He also had acute nasopharyngitis and tonsillitis.

"Treatment.—Vaccine administered, 200,000,000 staphylococcus aureus and 100,000,000 pneumococcus.

"June 3, no marked change for the better. Given 150,000,000 staphylococcus and 100,000,000 pneumococcus vaccine.

"June 5, feeling fine. Swelling gone down and could eat well. No vaccine administered. Discharged cured.

"Case 7. May 26, 1910. M. C. I., 39 years old.

"Complained of abscess of tooth and gums. Tooth was filled about a year previous. Became sore and sensitive all of a sudden. Filling removed, but trouble became worse. Gum was lanced by dentist May 24. No relief.

"Examination showed marked swelling of gums round affected tooth. Very little discharge present from lanced tooth. Cultures obtained for the preparation of autogenous vaccine showed at the end of 24 hours small chains of pneumococci, some staphylococcus aureus and a few long, thin bacilli.

"Treatment.—Was given 200,000,000 staphylococcus aureus and 50,000,000 pneumococcus vaccines.

"May 28, felt much improved. Swelling considerably reduced. Practically no pain. Given another injection of 500,000,000 staphylococcus aureus and 50,000,000 pneumococcus vaccines. Discharged cured. Did not need any further treatment.

"Case 8. Aug. 1, 1910. P. F. T., male, 44 years old.

"Complained of an 'acute abscess of lower left molar tooth. Nerve was devitalized and tooth filled when trouble started. Did not seem to get better under local measures.'

"Treatment.—Vaccines, 100,000,000 pneumococcus and 150,000,000 staphylococcus aureus administered.

"Aug. 3, suppuration stopped. Wound healing rapidly. Felt no pain on mastication. Was given another dose of 250,000,000 staphylococcus and 100,000,000 pneumococcus vaccine. Discharged cured. No further treatment was necessary.

"Case 10. April 15, 1911. S. W. E., female, 55 years old.

"This patient, whom I saw at her home in consultation with her dentist, complained of infected lower right cuspid. Had a fixed bridge put on two weeks before. Soreness began three days ago. Swelling of the gum and considerable pain. Could not sleep for the last two nights on account of pain. No fluctuation present.

"Treatment.—Given 250,000,000 staphylococcus aureus and 75,000,000 pneumococcus vaccine. 'Had a good night's sleep for the first time since trouble began' same evening.

"April 17. Swelling and pain subsided. Felt well otherwise. Given 200,000,000 staphylococcus and 100,000,000 pneumococcus vaccine. Discharged well. Bridge did not have to be removed."

He sums his experiences as follows:

"The cases of mandibular abscess cited, especially those accompanying a partially erupted tooth, are particularly instructive. They indicate what might be accomplished with vaccines in similar acute infections. According to the best text-books on Dental Pathology and Therapeutics such cases are the worst ones met with in dental practice. Local surgical treatment is practically impossible in such cases on account of the rigidity of the muscle and the locking of the jaws. The condition is therefore left to nature to do its best or worst, depending upon the virulence of the bacteria and the general condition of the patient, who has to fight his own battle practically unaided. The vaccine treatment which tends to raise the resistance of the patient against the invading bacteria is apparently the only direct help we can give the patient under the circumstances.

"The cases here recorded are probably the very worst ones met with by dentists. Practically never have I had a case referred to me unless the dentist was fairly satisfied that he could do little for the patient by local measures alone, or after such local treatment had been given a fair trial and failed. The results obtained are, therefore, more valuable.

"The records of all the cases that came under my observation have been cited in detail so that every one may be able to judge for himself and draw his own conclusions therefrom.

"The two chronic cases with fistulas were cited principally to call attention to the limitations of this treatment

and also to indicate that vaccines should not be expected to substitute local surgical measures when necessary.

"The number of cases are too few to draw definite conclusions from. I should like, however, to emphasize the following points:

"1. Vaccine treatment is of value in acute septic dento-alveolar abscesses—even the worst types of mandibular impacted third molar abscesses have apparently yielded well to this treatment.

"2. Such cases with septic apical abscesses, especially the deep-seated ones or the so-called blind abscesses, acute and subacute, have been greatly benefited by the vaccine method of treatment.

"3. I believe that there is a big field for vaccine treatment in acute and subacute dento-alveolar abscess cases and its widespread use will save considerable suffering and loss of teeth to the patient and annoyance to the dentist."

Vaccine application in mouth infections has been sadly neglected when we consider the great amount of suffering that can be avoided by this method. Morphine and other drugs are often resorted to in these cases, but they do not give the same measure of relief, nor do they have a curative influence, while vaccine inoculations do both.

From our present knowledge regarding the prophylactic value of vaccines in surgery there is no good reason to doubt that vaccines would be a very valuable adjunct to local treatment in procuring rapid healing of the gums after teeth extractions. The lacerated tissues from teeth extractions present a good field for infective processes and in many cases quite extensive infective processes take place. By giving vaccines after extracting the teeth in every case this painful inflammatory condition could be avoided.

PYORRHEA.

Pyorrhea is due to an infection of the peridental membrane, with a resulting absorption of the alveolar process, retraction of gum, and final loss of tooth unless the infective process is arrested.

Much bacteriological work has been done to determine the exact etiologic factor in this disease. The usual pyogenic organisms, streptococci, pneumococci, staphylococci and other germs usually found in infective processes of the mouth, are found in the pus procured from scraping in the space around the teeth.

The entamoeba buccalis has been considered a possible etiologic factor in this disease for some years. Smith and Berrelle, at a meeting of the Pennsylvania State Dental Society, July, 1914, announced that as a result of their investigations they considered this organism the real cause of the disease. About the same time and a little later, Bass ("Alveolar Pyorrhea," p. 22) found the entamoeba buccalis in 300 cases of unquestioned pyorrhea, while the organism was not found in control cases. He considers the entamoeba buccalis the real cause of the disease, because of its constant presence and from the clinical symptoms of improvement after killing of the organism with the use of emetin, one of the alkaloids obtained from ipecac, which has a specific poisonous effect on the entamoeba buccalis.

From this viewpoint, the pus organisms always found in the diseased tissues would be secondary invaders, entering after the entamoeba has destroyed the peridental membrane. Bass is of the opinion that these organisms cling to the entamoeba buccalis and are carried down into the tooth socket with them. He contends that entamoeba, by their continuous motile activities, disturb the granulating surface in the alveolar process and by this means dig up new soil, as it were, for the deeper penetration of the pus organisms, with a resulting gradual destruction and absorption of the alveolar process.

At all events, from a careful study of this disease, it must be quite clear that the diseased condition is due to the combined activities of the entamoeba buccalis and pyogenic organisms and that neither of these factors would cause

the same amount of destruction when operating alone. This fact, to my mind, has been clearly brought out by the immunizing and the emetin methods of treatment.

It can readily be seen that, where a comparative low resistance to streptococci or other pyogenic organisms exists, more rapid progress of the disease will take place under the combined influence of the entamoeba buccalis and the pyogenic organisms than where the pus organisms could not maintain themselves on account of a high immunizing resistance to them. In fact, there is good reason to believe that the entamoeba could not maintain itself, especially in the early stages of the disease, if the pus-producing organisms were not present as accomplices. The good results obtained from the use of vaccines in the treatment of pyorrhea, especially when used in the early stages, demonstrates this. In my own experience I have seen well-advanced cases cured with the use of vaccines. The good results from the use of vaccine in pyorrhea was recently seen in one of my employees. In this case the pyorrhea had been fairly well advanced. A dentist was consulted who took care of the teeth by the usual methods of cleansing and scraping, and without his knowledge I gave vaccine inoculations at the same time. The case improved rapidly and the dentist was surprised at the progress that was being made. In three months' time the pyorrhea was relieved without any apparent return of the disease.

My friend Dr. Thuner, of this city, (Bacterial Therapist, September, 1914) relates a personal experience that is quite striking. He says:

"I suffered with pyorrhea alveolaris for years, not only losing a number of molars but suffering from an infection which produced various constitutional disturbances. Dentist tried the treatments usually used without any permanent improvement. The disease would generally terminate by the loss of the teeth affected. The last trouble was with an upper front tooth, which I very much dreaded to lose.

The tooth was loose and my dentist informed me that he could not save it, but told me of Mrs. Eugene Smith having cured her pyorrhea with Sherman's vaccine. I asked Dr. Eugene Smith about it and he verified what the dentist told me. I started immediately and took injections of pneumococcus-streptococcus-staphylococcus combined stock vaccine. A curious thing took place about two hours after the injection. The tooth became very sore and started to bleed and bled for about one hour, but next day felt very much better. In about four days the soreness was nearly all gone and the tooth became firm again. I took altogether about six doses and am entirely relieved of the pyorrhea, and also wish to mention that I feel better in every way, undoubtedly due to the immunizing influence of the vaccine from which a normal resistance to these pyogenic organisms has been developed."

Many articles have appeared in medical and dental journals, giving experiences with the use of both autogenous and stock vaccines, which indicate the marked therapeutic value of vaccine in pyorrhea.

Allen ("Vaccine Therapy," fourth edition, p. 197) sums up the results from the use of vaccines in pyorrhea as follows:

"The results that are to be expected from a course of vaccine treatment depend on several factors: (1) The stage of the disease; (2) the skill and care which the dentist simultaneously devotes to the case; (3) the attention which the patient bestows on himself; (4) the length of time available for treatment. It also becomes necessary to decide in our minds what constitutes 'cure.' Inasmuch as the causal organisms are always present in the mouth, unlimited opportunities exist for reinfection, and this will inevitably occur unless the pre-existing conditions are obviated. In the earliest stages it is possible by dental and other methods to restore the gums to full health and vitality in the great majority of cases, perhaps in almost every case; but this condition will only be maintained by great care on the part of the patient, and occasional supervision by the dentist. Accumulations of tartar and of food debris must be prevented and the gums massaged daily.

"In all other stages—i. e., when once the gum has begun to lose its intimate connection with the teeth—reinfection is bound to occur sooner or later, unless extreme attention is paid to oral hygiene; in fact, it might almost be said 'once a pyorrhoeic always a pyorrhoeic.' It is this liability to reinfection that makes it so difficult to decide what constitutes 'cure.' It seems fair to agree that this term shall be applied when, six months after the cessation of treatment, (1) the teeth are quite firm in their sockets; (2) careful pressure reveals no pus and the probe no pockets between the gums and teeth; (3) the gum tissues are firm and healthy-looking; (4) there has been no further destruction of tissue, either of the gum or bony structures; (5) constitutional and general symptoms have not recurred.

"It is only by the earnest combined efforts of dentist, patient and physician that such results are obtainable, and it should be impossible to speak of the results of inoculation treatment alone, for no physician should allow himself to be persuaded so to neglect the principles of vaccine treatment as to rely on the use of inoculations only. It is the combined attack only which fulfils the requirements of vaccine treatment, and by its due delivery 'cure,' as defined above, should be obtainable in every case that is seen in the earliest stages, in the great majority of instances where the teeth are still firm and the bony structures as yet intact, even when constitutional symptoms are marked; but when the gums are spongy and destroyed to any great extent, the teeth loose, and the alveolar tissues eroded, amelioration alone is to be expected, and the maintenance of this will depend on constant supervision."

From the results obtained in the treatment of pyorrhea with vaccines, the pathogenicity of the pyogenic organisms associated in the infection becomes clearly evident, and furthermore, the apparently permanent results that are secured also indicate that the entamoeba buccalis can not successfully maintain itself in the peridental membrane when the soil is unfavorable for the growth of pyogenic organisms, especially so in the early stages of the disease.

The unquestionably good results that have been obtained from the use of emetin hydrochloride, hypodermi-

cally or into the pus pockets, as shown by Bass and others, is conclusive evidence of the pathogenic character of this organism in pyorrhea. Bass has found that in practically all cases the entamoeba disappears from the tooth sockets after a week's treatment with emetin. Concerning the results procured, Bass ("Alveolar Pyorrhea," p. 137) says:

"Though the specific emetin treatment causes the disappearance of demonstrable entamebae, the lesions or pockets remain and will require days, weeks, or months to heal, depending largely upon the size, extent and nature of the individual lesions as well as upon the natural healing powers of the individual patient. In many lesions there is considerable alveolar bone denuded of its periosteum, which, therefore, must be removed by the long, slow process of nature, if not aided by artificial, mechanical means. It requires nature several months to absorb and remove the alveolar bone after a tooth has been extracted, and it requires several months also to remove the alveolar bone above the level of the living peridental membrane in the case of pyorrhea. After the entamebae have been destroyed and the blood no longer contains emetin, these lesions or pockets offer the most favorable soil for reinfection."

It should be remembered that emetin, in the doses given to destroy the entamoeba, has practically no germicidal effect on the pyogenic cocci, and here the natural healing power of the patient depends largely on his ability to cope with the pus organisms present in the alveolar process and tooth sockets. That vaccines will aid the "healing powers" in the presence of an infection has been sufficiently demonstrated.

From these various considerations it would appear that the most rational procedure would be to employ emetin to get rid of the entamoeba buccalis and vaccines to hasten the healing process, by immunizing against the pyogenic organisms.

Emetin hydrochloride is marketed by drug houses in sealed ampules containing one-half grain each, ready for

use. The contents of the ampule are withdrawn into the syringe and injected intramuscularly, the usual antiseptic precautions being observed. Daily inoculations for one week will suffice. Where extensive pus pockets exist it may be necessary to flush them with emetin solution. For this purpose, emetin hydrochloride 1:10,000 will answer the purpose.

Vaccine inoculations should be made by employing a vaccine corresponding to the organisms present in the pyorrhea pockets, either stock or autogenous, usually streptococcus 20,000,000, pneumococcus 30,000,000, staphylococcus aureus and albus each 100,000,000, micrococcus catarrhalis 100,000,000, as the first dose. The dose should be repeated at five to seven-day intervals and the dose gradually increased to three or four times this amount and the treatment continued until the entire inflammatory process is relieved.

There has been much said and written concerning the importance of salivary calculus as an etiologic factor in pyorrhea. From our knowledge of germ activities in the production of renal calculi and gall-stones, there is no room for doubting that salivary calculi are the direct cause of deposits from pus formations. These crust formations should be carefully removed, because they are a direct source of a continuous reinfection and also mechanically irritate the gum.

CHAPTER IX.

INFECTIONS OF THE LOWER RESPIRATORY TRACT.

Lobar Pneumonia.

Pneumonia holds the record as being the cause of more deaths than any other disease. This is of itself sufficient evidence that the usual treatment of this disease is not adequate. In view of the uniform good results from the early administration of vaccine in pneumonia, the fact that this method of treatment has not come into general use can only be ascribed to the theoretical objection to the employment of vaccines in the early stages of extensive acute toxic infections. A better understanding of the workings of the immunizing process overthrows these theoretical objections and explains the clinical experience that in acute infections killed organisms, injected under the skin, stimulate more abundant antibody production than virulent organisms. Let us take up (1) why the virulent pneumococcus infections fail to arouse active immunization and (2) why vaccine injections succeed.

That the pneumococcus is the principal infecting organism in lobar pneumonia is now generally recognized, but during the past few years considerable discussion has taken place as to whether the pneumococci present in the mouths of normal individuals are identical with those isolated from the lungs in cases of virulent pneumonia. By means of serologic tests Dachez and Gillespie (Journal A. M. A., Sept. 6, 1913) and later Dachez and Avery (Journal of Experimental Medicine, 1915, XXI, 146) succeeded in demonstrating three different types of pneumococci distinguishable from one another, which were not found in the mouths of individuals who had not been exposed to cases of lobar pneumonia. They also found a fourth group that corre-

sponded to the pneumococci found in the mouths of normal individuals. From these investigations they conclude that about 75 or 80 per cent of the virulent types of lobar pneumonia are due to pneumococci of the first three types, and that from 20 to 25 per cent, usually the less virulent cases, are due to the pneumococci found in group four.

Dachez and Avery (Journal of Experimental Medicine, July 1, 1915) also investigated the length of time the virulent types of pneumococci persist in the mouth after recovery from pneumonia, and to what extent healthy persons exposed to pneumonia become carriers of the virulent types of pneumococci. They sum up their conclusions as follows:

"Lobar pneumonia in 75 per cent of instances is due to specific types of pneumococci possessed of a high degree of pathogenicity. Although pneumococci occur in the mouths of 60 per cent of normal individuals, such organisms are readily distinguishable from the highly parasitic types of pneumococcus responsible for the severe forms of lobar pneumonia, a convincing proof that infection in this disease is, in the majority of instances, not autogenic in nature, but is derived from some extraneous source. In a high percentage of instances, healthy persons intimately associated with cases of lobar pneumonia harbor the disease-producing types of pneumococcus. In every such instance the pneumococcus isolated has corresponded in type with that of the infected individual. Convalescents from pneumonia carry for a considerable length of time the type of pneumonia with which they have been infected. The existence of the carrier state among healthy persons and among those recently recovered from pneumonia establishes a basis for understanding the mechanism by means of which lobar pneumonia spreads and maintains its high incidence from year to year."

That these various types of pneumococci are closely allied, if not identical in their biochemical construction, is shown by the specific influence of ethylhydrocuprein hydrochloride on the pneumococcus. Moore (The Journal of Experimental Medicine, September, 1915, p. 284), after giving extensive experimental data, concludes in part as follows:

"Ethylhydrocuprein hydrochloride in very high dilution inhibits the growth of, and in eighteen hours kills, representatives of all four groups of pneumococci in vitro. The killing effect is generally seen in somewhat lower dilutions than the inhibiting effect. No constant or considerable difference is seen in these actions on representatives of the four groups of pneumococci. The action of ethylhydrocuprein hydrochloride on the pneumococci in vitro is so strongly specific that it may possibly be used as a test for a true pneumococcus.

The inhibitory or killing effects of ethylhydrocuprein hydrochloride in vitro on bacteria other than pneumococci are slight or absent. The effects are greater on streptococci than on any other organisms examined, but are still much less than on the pneumococci. This action distinguishes between the streptococcus group, including streptococcus mucosus sometimes found in normal mouths, on the one hand, and the true pneumococcus (including pneumococcus mucosus) on the other."

In clinical pneumonia we sometimes find, besides the pneumococcus, the streptococcus, Friedlander bacillus, influenza bacillus, or some other organism to be the principal infecting agent. The streptococcus, being a common invader of the respiratory tract, no doubt becomes a serious complicating factor in many cases.

The clinical manifestations of pneumonia are quite characteristic. When we are called to see a patient with a history of having had a cold for several days, followed by a chill, severe pain in the chest, cough, blood-streaked expectoration, fever, a bounding, rapid pulse, there is not much room to doubt that lung consolidation will soon follow. Some cases will present such symptoms and go on to recovery without developing typical pneumonia, but they seldom occur.

Why does an existing pneumococcus infection fail to arouse sufficient immunization? In the early stage of pneumonia the pneumococcus is readily found in the blood and in all probability the pneumococcus is present in the blood

for some days prior to the time the infection localizes in the lung. After consolidation takes place, if the case progresses favorably, the pneumococci steadily disappear from the blood, while at the same time they multiply very rapidly in the involved lung tissue. This is in accord with the general rule that infecting organisms, as long as they circulate only in the blood, do not appear to stimulate antibody production, and that active immunization is only developed after the infection has localized and tissue cells involved.

The toxic character of virulent pneumococcus infections is very pronounced, as shown by temperature, pulse rate, general depression, and often delirium, while the development of immunizing resistance is slow in proportion to the amount of toxic materials produced. Vaughan attributes virulence in pneumococcus infections largely to the rate at which the organism multiplies and believes this rate of multiplication is due to the effectiveness of the ferment which the organism secretes in preparing the food on which it lives. Evidently the organism's ability to secrete efficient digestive ferments safeguards it from rapid destruction, the toxic character of this ferment exerting a devitalizing effect on tissue cells with which it comes in contact.

Rosenow (Journal A. M. A., Sept. 7, 1912), in his work on the toxic character of pneumococcus infection, found that during the process of pneumococcus autolysis in normal salt solution a substance is evolved which has a very toxic influence and, when injected into animals, does not stimulate immunizing responses towards checking the progress of pneumococcus infections, but on the contrary seems to inhibit the immunizing mechanism. This same toxic material was also found in pneumococcic pleuritic effusions and in consolidated pneumococcic lung tissue. From this he concluded that in toxic pneumonias a continuous autolysis of the pneumococcus takes place, with the liberation of this poison, which plays no part in building up an immun-

ity, but rather retards or hinders antibody production. From our present knowledge of enzymes or ferments it is difficult to avoid the conclusion that this toxic substance is due to ferment production by the pneumococcus.

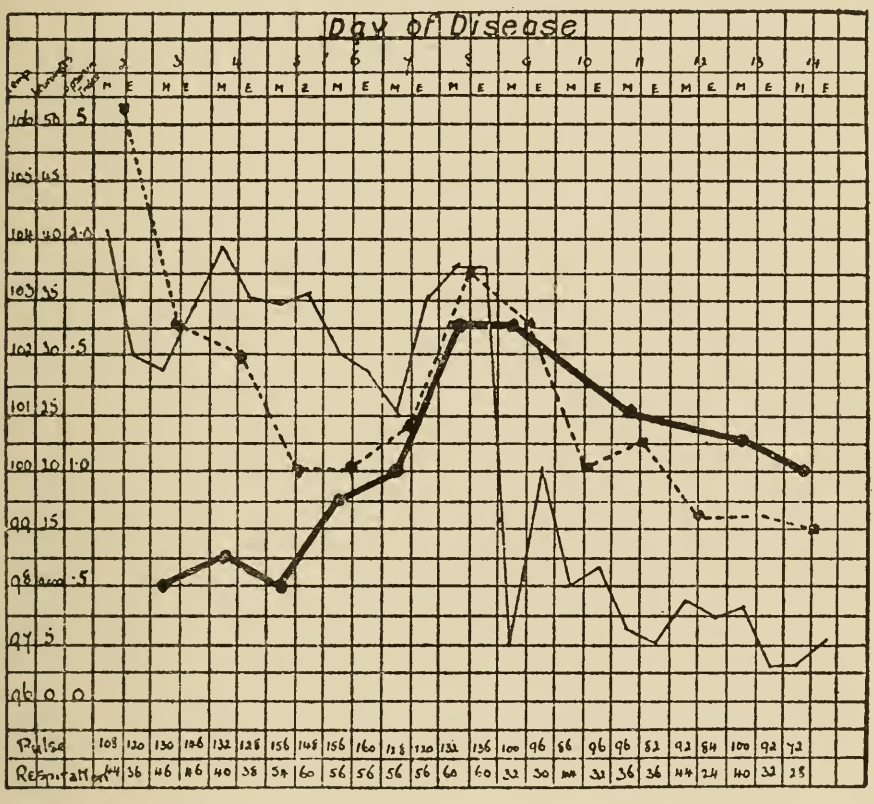
The presence of a large number of pneumococci in the blood at the time the infection begins to localize in the lung shows that the pneumococci possess some properties at this time which prevent the leukocytes from digesting them; that they possess a certain virulence which hinders the leukocytes in their attack, and temporarily demolishes the immunizing forces. Furthermore, active leukocytosis does not take place until some newly formed antibodies appear in the blood serum which sensitize, opsonize, or in some measure destroy the virulence of the pneumococcus. This is clearly shown by following the opsonic index during the course of an attack of pneumonia.

Eyre (Lancet, Feb. 22, 1908, p. 546), in referring to Macdonald's work, states that his investigations confirm the results obtained by Macdonald, showing that the formation of pneumococcic opsonin throughout the course of the disease indicates the movements of the curve representing the opsonic index and affords an exact record of the measure of resistance opposed by the patient to the inroads of the organism. They find that in cases where the opsonic index rises abruptly recovery takes place by crisis; where it rises slowly recovery takes place by lysis; and in fatal cases the opsonic index continues to go down. Eyre also shows a striking relation between the leukocyte count and the opsonic curve. In fatal cases leukocytosis is absent and the opsonic index falls gradually and constantly. In favorable cases the leukocyte count is high in the early acute stage and falls until before the crisis when it rises again with the index.

Chart I shows the relations of the temperature to the opsonic index and leukocyte count as the disease progresses.

These correlated findings clearly show that at the onset of an attack of pneumonia a pneumococcus has taken possession of the body, which resists destruction because of the efficiency of the ferments with which it digests and assimilates substances obtained from the animal body; that

CHART I.



RELATION BETWEEN LEUCOCYTES, OPSONIC INDEX AND TEMPERATURE IN A CASE OF PNEUMONIA. (EYRE.)

Dotted line equals number of leucocytes per cubic millimeter; thick line equals opsonic index; thin line equals temperature.

it circulates freely in the blood without apparent opposition by the leukocytes until some antibody finds its way into the blood serum which has a sensitizing or opsonizing influence on the pneumococcus; and that this antibody is not adequately formed until the micro-organism localizes in the lung and causes localized tissue involvement.

After localization of the infection in the lung tissue has taken place the degree of virulence of the infecting organism is the important factor in determining the progress of the disease. If the influence of the pneumococci on the involved lung tissue is such that sensitization for the production of specific ferments or antibodies for the destruction of pneumococci takes place readily, the infection will be aborted before much progress in lung involvement takes place. If, on the other hand, the pneumococcus, by its effective digestive and assimilating capacity and its ability to multiply and grow rapidly, irritates the involved lung tissues beyond the point of adequate resistance; if the virulence of the organism cripples or overwhelms the involved lung tissue so that antibody production is deficient, then extensive infiltration of the lung results. Inflammatory exudates spread so as to obliterate the air cells, solidify the lung tissue and impede the blood circulation, creating an admirable condition for germ development, even if adequate antibacterial substances are in the blood, because they no longer can circulate freely. If antibodies are found at the boundaries of the intensely inflamed area, where the irritating influence of the infecting organism is not so intense, they will find their way into the general circulation and there have a sensitizing or opsonizing influence on the pneumococci circulating in the blood so that phagocytosis can take place. It is for this reason that the pneumococci begin to disappear from the blood after lung involvement has taken place. But where the virulence of the pneumococcus for the individual is such that antibody formation is greatly retarded, so that the opsonic index remains low, a fatal termination is to be expected.

WHY BACTERIAL VACCINES SUCCEED IN AROUSING IMMUNOPRODUCTION.

It is clear that the most important factor in a case of lobar pneumonia consists in securing an adequate amount

of antibody production, if possible, before lung consolidation has taken place; if this is accomplished, enough blood circulation may be maintained in the congested and inflamed portion of the lung so that sufficient germ multiplication to cause complete consolidation becomes impossible. We have seen that living virulent pneumococci, on account of their irritating or depressing effect on the tissue cells, do not rapidly stimulate antibody production, and that with very virulent organisms this property of stimulating antibody production is actually absent. For this reason spontaneous recovery from pneumonia so rarely occurs. When, however, killed pneumococci are injected into healthy tissues, those remote from the infected lung are roused to produce antibodies. The organisms contained in the vaccines, being killed, no devitalizing influence on tissue cells like that produced by live organisms is manifested, and the entire cell energy is devoted to antibody production. In other words, the killed organisms are a far more efficient antigen than living organisms. In addition to this, instead of obliging the tissues in the infected area to bear the entire load of overcoming the infection, additional tissue is called into immunizing service at the site of inoculation.

Theoretically, the earlier the vaccine is employed the better the results, and this is verified by experience as shown where a dose of vaccine is given within several hours after the characteristic initial chill and repeated at daily intervals for three or four doses. Under these circumstances lung consolidation is usually avoided; a crisis is, as a rule, precipitated within 24 to 36 hours with a drop of temperature, abatement of toxic symptoms, improved heart action, a normal temperature within three to five days, with a resulting rapid recovery.

Let us now take up the objections which have been made to vaccine treatment in pneumonia. The question has been raised whether vaccine injections would not do harm in

extremely toxic cases, because, by injecting killed germs, toxic material is added to a system already overloaded with toxic material. This objection does not hold good, because the toxic material in a dose of vaccine is so small that it amounts to nothing compared to the toxic substances that are constantly being evolved by the live organisms. If the injected vaccine had a toxic influence, a noticeable rise of temperature with other toxic symptoms would follow within a few hours after giving the vaccine, but no rise of temperature that can be ascribed to the vaccine takes place. In fact, toxic cases of pneumonia tolerate comparatively large doses without toxic reaction, and inoculations can be made at short intervals to advantage.

Pneumonia being due to several types of pneumococci that are immunologically distinguishable from one another, it is important that the stock vaccine should be polyvalent and consist principally of the virulent strains. A polyvalent vaccine not only meets the infecting organism by its own type, but also exerts immunizing influences by group action. While there are a variety of pneumococci, there is abundant evidence that they are biochemically closely allied and that there is an overlapping in the immunizing responses to the various strains. By a polyvalent vaccine, the offending organism is attacked by immunizing efforts from different angles. From my experience in applied immunologic therapeutics, there is good reason to believe that this group action of vaccines extends from the various types of pneumococcus even to the streptococcus. This may be accounted for on the ground that these two organisms are closely allied.

CHOICE OF VACCINE AND DOSAGE.

The streptococcus is so frequently either a complicating or a primary factor in respiratory infections that the addition of the streptococcus to a pneumococcus vaccine for the treatment of pneumonia is of distinct advantage. By this

means we get the benefit of the group action of the streptococcus in the vaccine on the pneumococcus infection, and at the same time immunize against streptococcus infections. From extensive clinical observation in the treatment of pneumonia, I am convinced that a combined pneumococcus-streptococcus vaccine possesses marked therapeutic advantage over a straight pneumococcus preparation. Many physicians prefer to use a combined vaccine containing a staphylococcus in addition to the pneumococcus and streptococcus and from what experience teaches, with the use of this combination, there is certainly no evidence that the addition of the staphylococcus is of any disadvantage.

The initial adult dose should be about 60,000,000 to 80,000,000 each of polyvalent pneumococci and streptococci and if staphylococci are also a part of the combination, 200,000,000 of this organism may be included. The same dose should be repeated the next day. In the early stages of the disease, if the case shows severe symptoms, two inoculations should be given the first day, and if marked improvement does not take place two inoculations may be given the second day. After the severe symptoms have subsided and the temperature approximates the normal mark, inoculations should be made at daily intervals for about two days, and at three to four day intervals after that until complete recovery has taken place. If treatment is started early a normal temperature should be expected in less than five days with but comparatively few exceptions.

If the case has advanced to extensive lung consolidation such rapid progress should not be looked for. The blood supply to the consolidated lung in this condition is very limited and even if antibodies are present in the blood they will not reach the solidified portion of the lung in sufficient amount to rapidly eliminate the infection; there may always be portions of the lung that have only reached the congestive stage, and by increasing the immunizing substances in

the blood, inflammatory extensions may be avoided; dosage and intervals between inoculations should be the same as when the vaccine is employed in the early stages of the disease. When used in advanced cases, as a rule, recovery takes place by a favorable lysis instead of crisis, but in some cases that are far advanced a dose of vaccine often seems to precipitate a crisis. Unfortunately when the vaccine is used late in extremely toxic cases the results are not so uniformally good, but even in these cases all hope should not be abandoned. I have on several occasions seen what appeared to be a hopeless condition make rapid improvement after vaccine inoculation and go on to recovery. A recent experience serves as an illustration: Dr. George A. Trizisky of Detroit, who had charge of the case, kindly furnished the data for the purpose of making this brief report. A girl, age 18. The doctor first saw her on Oct. 25, 1915. She had been sick three days. Temperature 101, pulse 120, respiration 18 to 20. There had been no chill, lungs clear, no particular pain, appetite indifferent, anaemic in appearance. There was no material change in the condition of the patient for three days. On Thursday, Oct. 28, she was found much worse, temperature 104, pulse 140 to 150, cyanotic, lips and fingers blue and very pale in appearance, respiration 30, pneumonia of right lung. Condition remained about the same for 24 hours. On Friday evening Dr. Trizisky called me over the phone for the purpose of considering the advisability of giving vaccines to this case. At that time the temperature was 104, pulse 150, respiration from 30 to 32. Consolidation of almost entire right lung and active congestion of lower portion of left lung, lips and fingers blue and general condition of patient bad. I advised 1 c.c. of a stock vaccine containing pneumococcus 80,000,000, streptococcus 60,000,000, staphlococcus aureus and albus each 200,000,000 to be given at once, which was done. The further course of vaccine treat-

ment was determined by daily consultation over the phone for several days. Saturday evening, Oct. 30, temperature 102, pulse 140, respiration 28, still cyanotic. No material extension of the inflammatory process in left lung. One c.c. of the same vaccine given. Sunday evening, temperature 101, pulse 130, and better in quality. Monday morning temperature 100, pulse 125, the same vaccine repeated. Monday evening temperature normal, pulse 120, and general conditions of patient much improved. After this rapid progress towards recovery took place.

Where a doctor wishes to use an autogenous vaccine it is necessary to procure a culture at once, because there is no time to loose, and have the vaccine prepared as soon as possible. Meantime the combined stock vaccine should be employed. As a rule, however, the patient progresses so favorably under the stock vaccine that it becomes a question whether the autogenous vaccine will serve a better purpose.

EXTRACTS FROM GENERAL LITERATURE.

A communication by Dr. Wynn which appeared in the Lancet (London) Jan. 31, 1914, is so clearly to the point that it deserves reproduction here.

THE USE OF VACCINES IN PNEUMONIA.

"TO THE EDITOR OF THE LANCET:

"Sir—The prevalence of pneumonia at the present time makes Sir R. Douglas Powell's letter in The Lancet of Jan. 24th of timely interest. It is to be hoped that those who have used vaccines in this disease will respond to his appeal for an expression of opinion. His own practice, of suggesting that a vaccine should be prepared from the sputum early in the attack, to be used in the event of continued severity or relapse of symptoms, and in some cases of slow resolution, probably represents that of most physicians. Vaccines are used as a last resort in cases doing badly.

"My own practice is to regard every case as a possibly fatal one and to give a vaccine as early as possible after the onset of symptoms. Little immediate good can be expected when consolidation is present, for antibodies cannot penetrate into the solid airless lung. However, since all the lung

is not in the same stage and parts may be in the condition antecedent to consolidation, good sometimes results. In the early stages of the disease before consolidation we are dealing with a septicæmia, and a vaccine then gives striking results. In a few cases I have been fortunate enough to give a vaccine within 24 hours of the initial rigor, in one case eight hours after the rigor. In these cases there has been an immediate response, and the aftercourse of the disease was profoundly modified. Usually the temperature fell to normal on the second or third day of the disease. In the case injected eight hours after the onset there was no further rise above 98.8 degrees F., although consolidation occurred. Generally after the first fall the temperature rose again to a moderate height, and finally fell to normal after a second dose of vaccine. A recent case may be given as an illustration. A man, aged 46, had a severe rigor at 7 p. m. on Jan. 10th and his temperature rose to 105.2 degrees. He was seen by me in consultation exactly 24 hours afterwards. His temperature then was 103.6 degrees, respirations 32, pulse 116, rusty sputum, soft mitral systolic murmur. The only physical sign in the lungs was characteristic subdued breathing at both bases. His general condition was flabby, and we regarded him as a distinctly bad subject for pneumonia. A dose of 30,000,000 stock vaccine was given at once. At 6 o'clock the next morning the temperature was 100 degrees, pulse 96, respiration 24. On Jan. 13th, 36 hours after the injection, the temperature was 98 degrees, pulse 72, respiration 24. On the 14th the temperature rose again to 103 degrees, pulse 108, respiration 40. Bronchial breathing was now present at both bases. A second dose of an autogenous vaccine containing 50,000,000 pneumococci and 50,000,000 micrococcus catarrhalis was now given. The temperature fell to normal next day and remained constantly normal. He was sent away to the seaside exactly 14 days after the initial rigor.

"So striking have been the results when vaccine was injected early that I would urge the adoption of this practice. The amount of consolidation is probably determined by the events of the first few hours of toxic invasion, yet a consultant rarely sees a patient at this stage when so much could be done. It may be argued that if cases are injected early there is no proof that the cases really had acute pneumonia. But the sharp rigor, dry hot skin, rusty sputum,

pulse and respiration ratio, and general appearance of the patients could scarcely be due to any other disease. It is an interesting point that in cases injected early consolidation may develop, although the temperature and pulse-rate are little above normal and the patients do not feel ill. The general symptoms improve out of proportion to the local disease. But it is unnecessary to wait for consolidation before making a diagnosis and giving a vaccine any more than one waits for the report on the throat swab before giving diphtheritic antitoxin.

"If a vaccine is given at the commencement of the disease it must be a stock one. Owing to differences in strain it is advised that this should be a polyvalent vaccine. But the difference between strains is mainly one of virulence, and my own practice is to use a vaccine from a culture of high virulence. For some time I have been using one derived from a rapidly fatal case of pneumococcic meningitis. When possible I make an autogenous vaccine for each case, but I am not convinced that such a vaccine has any advantage over a stock vaccine from a virulent culture except when the infection is mixed. Many recent cases have shown the micrococcus catarrhalis, but even then one can assume that the pneumococcus is the predominant organism.

"Unsuccessful results have been obtained by the use of inadequate doses. Doses of 5,000,000 to 10,000,000 are quite useless. My own doses have ranged from 25,000,000 to 50,000,000, and with increasing experience I find myself inclining to the larger dose. I have not used more than 50,000,000 as an initial dose, but I now think that this dose may be too small to abort the disease, and that a still larger dose would give better results. Sir A. E. Wright has found small doses frequently repeated absolutely ineffective, and suggests that a dose of 500,000,000 might be tentatively employed at the outset of a pneumonia attack. The fear of a negative reaction has prevented many from using vaccines in pneumonia. I have never detected clinically any signs of a negative reaction after the doses I have used. Sir Almroth Wright, in connection with his prophylactic inoculations, gives reasons for thinking that this stage may make default in the uninfected person and in the early stages of infection with doses of less than 1,000,000,000 of a pneumococcic vaccine, which is with difficulty broken down in the

body. If this fear can be abolished the way will be open for a more extensive use of vaccines in acute diseases.

"Probably no physician has had a sufficient number of cases to furnish satisfactory statistical evidence, and such evidence as can be brought forward may fail to convince others who have not seen the case which furnish it. But individual expressions of opinion may, I hope encourage others to use vaccines promptly in this fatal disease.

"I am, sir, yours faithfully,

"Birmingham, Jan. 25th, 1914. William H. Wynn."

The remark made by Dr. Wynn that the consultant does not see pneumonia cases early enough to obtain the best results applies equally to hospital practice. Most cases of pneumonia that are sent to hospitals are far advanced or are sent there as a last resort when unfavorable symptoms develop, but even these cases are benefited. The effect of precipitating a crisis after a dose is well illustrated by the cases reported in the North American Journal of Homeopathy, Jan. 1914, by E. P. Swift, M. D.:

"My first use of Pneumonia Bacterin was on a woman of 50 in which the disease involved both lower lobes, with pleuritic inflammation on the right side. She had passed the sixth day without signs of crisis or any favorable symptoms, respirations were 36 to 40, pulse rate 110 to 120, temperature 102 to 104, was semi-delirious and altogether an unpromising subject. An injection of 10,000,000 was given on the afternoon of the seventh and repeated on the morning of the eighth day. At noon of the eighth day the temperature had declined to 101, but the pulse rate had increased to 140 and respirations to 50. At 12, midnight, the temperature had declined to 99/4, pulse to 105, and respiration 48. There was gradual improvement in all symptoms after that, until at the end of the second week convalescence was fully established.

"Case 2.—J. N., admitted to Flower Hospital, Jan. 16, 1913. Double lobar pneumonia, complicated with chronic emphysema. Expectoration bloody, temperature 102 on admission, 105/3 on second day, respiration 28 and labored. On third day temperature was 105/1, pulse 120, respiration 42, patient sleepless and restless and looked bad. 50,000,-

000 vaccine were given at this time and the injection was immediately followed by defervescence as shown on the chart. The pulse rate was slightly increased for a few hours after the injection, but no other signs of reaction were apparent. Patient was fully convalescent on the sixth day.

"Case 3.—F. F., age 35, admitted to Flower Hospital Jan. 17th, 1913. Right lobar pneumonia, temperature 104, pulse 100, respiration 36, sputum bloody with pneumococci present. 50,000,000 vaccine was administered on second day with temperature at 104, pulse 115 and respiration 48. The temperature declined promptly, respirations were slightly increased for a few hours, but there were no other signs of reaction, and convalescence was established with practically normal pulse and temperature by the morning of the fourth day.

"Case 4.—Admitted to Hahnemann Hospital, Dec. 31st, 1912, under care of Dr. Hassler and reported here by his permission.

"Mrs. E. W., age 40, temperature on admission 103, increasing the same afternoon to 104, pulse 130, respiration 30 to 40. Lobar pneumonia.

"Fifty million bacteria were administered on the fourth day at 3:30 with temperature 102/5, pulse 110, respiration 32 to 40. Following the injection the temperature rose at midnight to 103/4 and respiration to 48, the pulse rate remaining unchanged.

"There was then a rapid decline to 100/4 at 8 a. m. and 99/4 at noon of the following day, with uninterrupted convalescence.

"It may, of course, be said that in all these cases the disease may have reached a turning point and that the prompt improvement in the last three reported cannot be proved to be the result of the use of vaccine, which is true, and a larger number must be studied before a positive conclusion can be reached."

Major W. N. Bispham (Military Surgeon, 1913, Vol. 32, p. 560) reports an interesting series of cases which aptly illustrates the influence of vaccines when used in various stages of the disease as follows:

"Immediately after a diagnosis is made, the primary injection is administered. On the following day, if the patient improves, no treatment is necessary, but if the temperature

remains high and the case is sthenic, an increased amount may be given at this time. On the third day, if the patient does not show sufficient abatement of symptoms, give another inoculation. This method of grading the treatment by observing the clinical symptoms must be adhered to, though if opsonic counts could be taken, such observations would be a valuable check on the work.

"A summary of my cases is as follows:

"Case I. M. C. 3203. An extremely severe case, temperature rising up to 104.6 degrees. Lower right lobe and apex of left involved. Pericarditis. He was treated symptomatically. Only slight amelioration of symptoms followed by death on sixth day. Autopsy confirmed the diagnosis.

"Case II. M. C. 2665. A fulminating case. Temperature 104.2 degrees on entrance. Examination disclosed consolidation of lower right lobe. Pneumococcus and Pfeiffer bacilli present in large numbers. Blood count gave 90 per cent polymorphonuclears. He was treated symptomatically, with crisis on the fifth day. Had an uneventful convalescence.

"Case IV. W. A. B. Prison Guard. A long continued case with recovery by lysis, but of only moderate severity. The right lower lobe was involved. His temperature was high (104.) degrees, but his general condition was good. Large numbers of pneumococci were found in his sputum. His differential blood count showed 85 per cent polymorphonuclears. He was treated symptomatically, with complete recovery.

"Case V. M. C. 3480. A moderately severe case. The lower left lobe was consolidated on entrance. His temperature ran to 104.2 degrees. Pneumococci were present. On the second day of the disease he received 50,000,000 pneumococci followed by 100,000,000 the next day. Crisis occurred the next morning on the third day of the attack.

"Case VIII. M. C. 3228. A mild case. Examination showed right lower lobe consolidated. Pneumococci present in sputum. Blood count gave 95 per cent polymorphonuclears, which percentage gradually decreased as treatment was pushed. His temperature never rose above 103.6 degrees after the first day. He received 50,000,000 on the fifth and sixth days, followed by crisis on the ninth day.

"This case shows decidedly the effect of delay in administering the vaccine. It is questionable whether it influenced his recovery in any material way.

"Case IX. M. C. 3724. A severe case. Examination showed consolidation of upper right lobe. Temperature rose to 105 degrees day after admission. Sputum loaded with pneumococci. He received 50,000,000 pneumococci on second day, million on third day, 100,000,000 on fourth day and 50,000,000 on sixth day, with crisis on sixth day. After the first dose the temperature never rose as high as before.

"Case X. M. C. 3719. A severe case. Involvement of lower right lobe. Temperature of 104 degrees was fairly constant. Pneumococci present. Received 50,000,000 pneumococci on second day, 100,000,000 on third day, 100,000,000 on fourth day, 200,000,000 on fifth day. Amelioration of symptoms was noted several hours after each dose. Recovered by lysis.

"Case XI. 3886. Very severe. Lower left lobe involved. Temperature on admission 106 degrees. Pneumococci present in sputum. Received 150,000,000 pneumococci immediately with prompt fall in temperature to 100 degrees, followed by no subsequent rise. Lung cleared up very rapidly.

"Such a case shows very markedly the prompt effect of these injections and also the need of early administration of the vaccine.

"Case XII. M. C. 3346. A very severe case. Right lower lobe consolidated. Temperature rising to 104.8 degrees. Differential blood count showed 92 per cent polymorphonuclears shift to the left (Arneth classification). Pneumococci present in large numbers. Gave 50,000,000 pneumococci on third day with resultant fall in temperature of 2 degrees; 100,000,000 on fourth day followed by fall of nearly 3 degrees; 100,000,000 on fifth day with fall of 2 degrees. Convalescence after that very rapid.

"Case XIII. M. C. 3495. Very severe attack. Lower right lung involved. Temperature steady at 105 degrees. Pneumococci present. Differential blood count showed 9 per cent polymorphonuclears; 50,000,000 pneumococci injected on third day; 100,000,000 million on fourth day and 100,000,000 on sixth day with crisis occurring twelve hours later.

"In this as in the preceding case every injection of the vaccine showed an immediate fall in temperature of from 2 degrees to 3 degrees.

"Case XIV. E. R. Prison Guard. Examination showed right lower lobe affected. Temperature rose to 104.4 degrees. Pneumococci present. Differential blood count showed 95 per cent polymorphonuclears; 50,000,000 pneumococci injected on first day; 100,000,000 on second day; 100,000,000 on third day. Crisis on fourth day. Convalescence uneventful.

"Case XV. M. C. 3477. A mild case. Right lower lobe consolidated. Temperature slightly above 100 degrees. Differential blood count showed 91 per cent polymorphonuclears. Pneumococci present in sputum; 50,000,000 pneumococci given with immediate convalescence.

"Case XVI. M. C. 3535. A moderately severe case. Left lower lobe involved. Temperature rose to 104 degrees. Pneumococci very abundant in sputum; 100,000,000 pneumococci injected on second day; 100,000,000 on third day; 100,000,000 on fourth day; 100,000,000 on fifth day. This last dose was followed by immediate crisis.

"Case XVII. M. C. 2797. A severe attack. Lower right lobe consolidated. Temperature rose to 104.6 degrees. Pneumococci present. An immediate relief of symptoms occurred on injection of 50,000,000 pneumococci.

"Case XVIII. M. C. 3083. A severe case. Lower left lobe affected. Pneumococci present in large numbers. Temperature rose to 105 degrees; 50,000,000 pneumococci were administered on the second day and 100,000,000 on the fourth day, followed by immediate crisis.

"The immediate fall of temperature after the injection of each dose of the vaccine, together with the great relief from the distressing symptoms, such as severe pain and dyspnea, was very marked, and impressed all of the medical attendants with the value of the treatment.

"It is well to note that none of these cases treated by the vaccines received other treatment, though stimulants were administered when thought necessary.

"Though this series is small, still I have thought it worthy of report as confirming the results obtained by other observers."

Dr. Henry A. Craig (Medical Record, Dec. 27, 1913), in speaking of the importance of early treatment, says:

"The early administration of a proper vaccine can hardly fail to be productive of good in a large percentage of the cases. The writer has had a number of cases where the vaccine was given within a few hours of the initial chill, and though the diagnosis was beyond question, the whole process was over in 48 or 72 hours. Many other observers have reported similar occurrences. * * *

"The best method of procedure, though all observers do not agree to this, is to administer a polyvalent stock vaccine of the pneumococcus and streptococcus, of each 30,000,000, at as early a date as possible. Make sputum smears and cultures, blood cultures in early cases, lung puncture in late ones, and proceed to the preparation of an autogenous vaccine. If there is no definite response in 24 or 48 hours, repeat or preferably give an autogenous vaccine. If there is no response in 36 or 48 hours, double the dose. If there is a response, as evidenced by improved clinical symptoms and signs, increased well-being of the patient, etc., defer reinoculation three days or until the first symptoms of retrogression in the general condition or the physical signs occur. Maintain the dosage or increase it every two or three days until the patient is entirely well. Generally about three doses are necessary."

Dr. W. C. Wolverton (The American Journal of Clinical Medicine, June 1, 1914), who has had extensive experience in the treatment of pneumonia, reports some cases among which the following are illustrative:

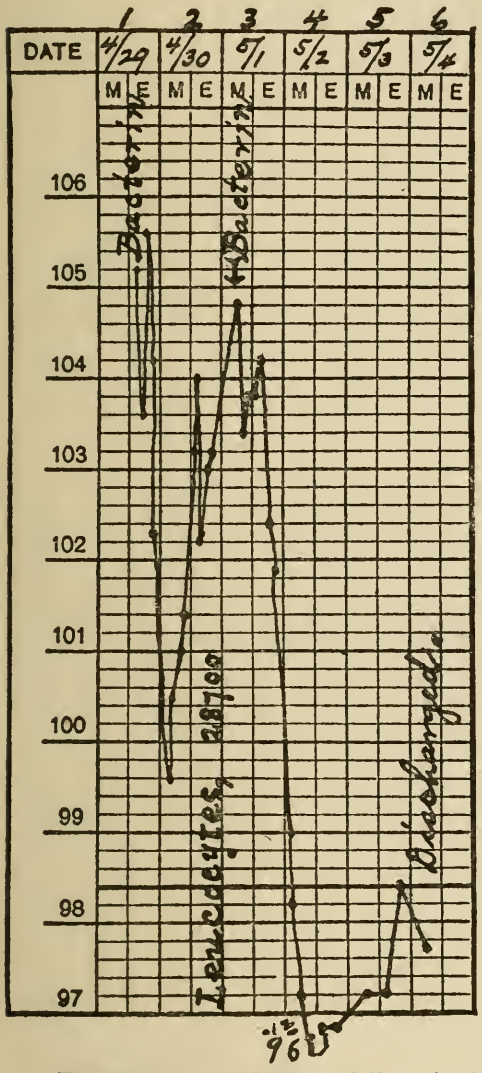
"In spite of the multitude of 'treatments' elaborated for his undoing, pneumonia remains the 'boss killer' in his season. A few years ago the writer believed that it would be a long time before any line of treatment would be evolved that would be superior to a routine of aconitine, veratrine, digitalin, strychnine, calomel, inunctions of guaiacol and camphorated oil, a cotton-lined jacket, besides a few other remedies for individual cases, as the need might arise. However, since adding the employment of bacterins to the foregoing line of treatment, his results have been infinitely better, and he has lost but one patient suffering from this disease; and in this fatal case the environment was such as practically to preclude recovery under any form of treat-

ment. Recently he has had under care at one time eight patients with pneumonia, and all recovered under treatment with bacterins, in conjunction with the usual indicated remedial measures.

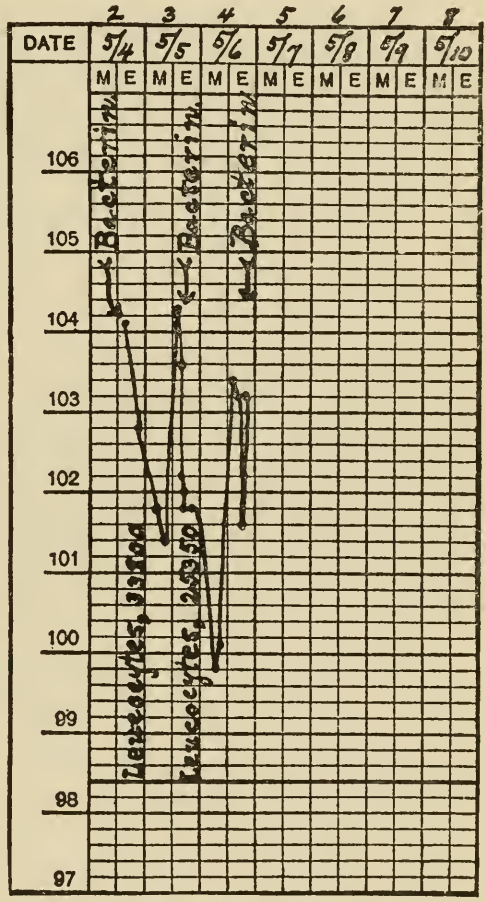
"On April 29, 1914, the writer first saw a case which well illustrates the possibilities of the bacterins in pneumonia when the doctor is called reasonably early. She was a Scandinavian girl of 12 years. A little over two months ago she underwent an operation, under the writer's hands, for the removal of a gangrenous appendix. She was anemic and in very poor physical condition at that time; but, with the 'Murphy drip,' Fowler position, free drainage, and the administration of the 'Van Cott' bacterin, she made a good recovery, leaving the hospital three weeks after operation. On April 29 the writer was called to see her, when he found her with a well-developed pneumonia of the right lower lobe. Temperature was then, at 3 p. m., 105.2 F.; pulse, 132; respiration was not counted, but was very rapid and shallow and accompanied by severe pain in the right side of the chest. She had had the initial chill and 'pain in the side' that same morning, some seven or eight hours earlier. She was coughing frequently and expectorating blood-streaked sputum. There was dullness over the entire right lower lobe. Her stomach was very irritable and she vomited all medicine given by mouth.

"A dose of a stock bacterin containing 24,000,000 killed pneumococci and 18,000,000 killed streptococci was administered at 3 p. m. Within an hour or two the temperature fell 1.6 degrees, but rose again to 105.6 at 8 p. m. Then the temperature began steadily to fall, reaching 99.6 at 5 a. m., with a pulse of 100. Next day, May 1, the morning temperature had reached 104.8 degrees and the pulse was 115. A second dose of bacterin, identical with the first, was now injected, whereupon the temperature began to fall within five hours, and went down uninterruptedly, reaching 96.2 degrees F. at noon of May 2, only 70 hours after the administration of the first dose of bacterin. The temperature was normal on the third day of the disease and remained so, the patient being discharged and returning to her home on May 4.

"The accompanying charts show graphically several things: (1) The high temperature at the time of each inoculation with the bacterin; (2) the sudden drop of 1 to 1½ degrees quickly following the inoculation, with as rapid return to about the original level, this marking the brief



Temperature chart—child of 12.



Pneumonia—girl of thirteen

Pneumonia—girl of 13.

negative phase; (3) the steady and continued drop in temperature, immediately following the short negative phase, characterizing the positive phase, this drop amounting, in the first instance to 6 degrees, and in the second to 8 degrees; (4) the gradual return of the temperature to near its former level, as the response of the immunizing mechan-

ism to the bacterin wore off, and the protective substances elaborated, consequent upon the inoculation, were used up in the war upon the invading bacteria, this being the indication for another dose of bacterin; (5) the typical crisis following the second inoculation, the temperature going considerably subnormal and not rising above the normal thereafter. In many cases, following the use of bacterin in pneumonia, the typical crisis seen here is absent, the disease ending by lysis.

"Another illustration: A German-Russian boy of 13 years entered the writer's private hospital on April 16, 1914. Another physician had made a diagnosis of ruptured appendix, and advised immediate operation. Careful physical examination, however, proved negative as to the abdomen, the tympanites and abdominal pain being caused by a collection of fermenting undigested sauerkraut in the colon; all abdominal symptoms disappeared after the administration of an enema.

"The real trouble turned out to be pneumonia of the left lower lobe. The temperature at the time of admission was considerably above 105 degrees F. The chart of this case unfortunately has been mislaid, so the exact temperature cannot be given. The patient was extremely toxemic, being delirious a great deal of the time. . This boy was in the fourth day of the attack when brought to the hospital, hence 'aborting' the attack was out of the question.

"Three doses of bacterin were administered to this patient, at about 48-hour intervals; smaller doses were given than would have been used had he been seen earlier, the extreme toxemia being considered a contraindication to full dosage. A blood examination showed a leukocyte count of 44,600, with 95 per cent polymorphonuclears; this blood-picture was the only hopeful aspect of the case. In spite of the late stage of the disease when the patient was first seen, and in the face of so extreme a toxemia and the existence of marked malnutrition, there was a very gratifying amelioration of the clinical symptoms following each dose of bacterin; the temperature in each instance would drop several degrees, the pulse slow down, from a rate of 130 to 150, to 100 to 110 beats per minute, and the mind would clear up completely for several hours. The disease finally

ended by lysis, which I believe was greatly preferable, in this case, to the typical crisis, for the boy had a complicating endocarditis, besides being in an extremely weakened condition generally. There is little doubt that this patient would have died had not the bacterins been resorted to.

"Another boy, also a German-Russian, of 11 years, was brought to the hospital on April 19, 1914, about 24 hours after the onset of a typical pneumonia involving the left lower lobe. His case appeared to be one of average severity, his temperature being in the neighborhood of 103 degrees F. at the time of admission. A dose of a stock pneumostreptococcus bacterin was injected, and, contrary to expectation, the temperature receded to normal within three days, the patient returning to his home on the fifth day after the onset of the attack.

"One more case of lobar pneumonia seems worthy of note, and will be cited, to illustrate the action of bacterins in this much-dreaded disease. The patient is a German-Russian girl, 13 years of age, who is at present under observation in this hospital. She was admitted on the afternoon of May 4, two days ago, at which time her temperature, as shown on the accompanying chart, was 104.1 degrees, and a pulse of 140. She has a pneumonia involving the right lower lobe. About three weeks ago she had a similar attack, involving the left lower lobe, for which she was treated by another physician, but who does not employ the bacterins in his practice. The case dragged along for quite a while, and the girl had experienced only one good day when this second attack began, on the morning of May 4. The lung originally affected has not yet entirely cleared up, consequently the prognosis in this case was guarded at the time of the first examination, a little over two days ago.

"A dose of bacterin containing 24,000,000 pneumococci and 18,000,000 streptococci was administered at 4 p. m. of the 4th, when a fall of not quite 3 degrees in temperature resulted (no antipyretic drugs were administered); but about 24 hours later the fever had reached its former level. Believing that in this instance the initial dose of bacterin had been too small to be productive of lasting good, a second dose, containing 32,000,000 pneumococci and 24,000,000 streptococci, was injected at 6 p. m. of May 5. This

morning (May 6) the temperature was 99.8 degrees F., pulse 108. The fever then gradually rose, reaching 103.4 degrees at 1 p. m. At 6 p. m., today, it had again begun to fall, owing, undoubtedly, to the development of a positive phase following the dose of bacterin given 24 hours ago. The time to give a dose of bacterin, following a prior dose, is before the positive phase excited by the prior dose has passed off; so, a third dose, containing 12,000,000 pneumococci and 9 million streptococci, was injected at 7:40 p. m.

"From present indications there should be a normal or a subnormal temperature in this case within the next 24 to 48 hours. The reason for taking up this last case at such length is to show that even in the most severe cases the bacterin not only is harmless, in therapeutic dosage, but causes a distinct amelioration in the clinical symptoms. These patients almost invariably will tell you of a feeling of well-being (euphoria) within 24 hours after each dose of bacterin has been administered."

There is no doubt that pneumococcus vaccine will increase the opsonic content of the blood. This has been abundantly demonstrated. Dr. R. W. Allen, of London, ("Vaccine Therapy," third edition, p. 117) says:

"We are therefore limited, in our endeavors to find a truly scientific method of treating cases of pneumonia, to increasing the amount of opsonin; and this, as has been already shown, can be effected by injections of a vaccine, best of the patient's own bacteria; the benefits thereby secured are so immediate and so great that the author has little diffidence in asserting that the space of a few years will see all cases of pneumonia treated by this method.

"A weak, irregular, very rapid pulse, enfeebled constitution, low muttering delirium, dry furred tongue and sordes about the lips, are of course unfavorable signs; yet so marked has been the improvement, even after one injection, in two cases of this type, that no case is to be looked upon as hopeless."

"Butler Harris, from a study of eleven cases of pneumococcic lung infections treated with vaccine, concludes:

1. That successful inoculation for pneumonia is possible.

2. That inoculation does no harm.

3. That a vaccine from one or a number of virulent strains should be used.

4. That it should be introduced as early as possible.

5. That indical control is unnecessary.

6. That temperature and physical signs are sufficient guide.

"The advantages, then, to be claimed for routine treatment by vaccines in all cases of pneumonia are: Precipitation of the crisis; diminution, therefore, of the risks of heart failure and other toxemic symptoms; increased comfort of the patient, and diminished liability to such sequela as empyema; curtailment of the whole course of the disease to a fortnight, or even less.

"In chronic or unresolved pneumonia the exhibition of a vaccine is the treatment par excellence. An initial dose of 25,000,000 may be increased subsequently to 50,000,000, control for dosage and intervals between the injections being furnished by (1) auscultatory signs, (2) careful microscopy of the sputum for bacteria and varieties of cells present; (3) general condition of the patient."

On the value of pneumococcus vaccine Dr. W. H. Watters (New England Medical Gazette, September, 1910, p. 419) says:

"Any conclusions that are drawn concerning the value of this form of treatment in pneumonia must be of questionable value unless they are based on the changes from severe illness to comparative comfort and convalescence. * * * It must be said, however, that such favorable alterations occur with pleasing frequency after suitable inoculations and that many of our clinicians believe that not a few apparently hopeless cases have been saved by this method of treatment."

Dr. F. E. Stewart (Journal A. M. A., May, 1910, p. 1824) holds "that the pathologic condition resulting from an acute

pneumococcic infection can be relieved, removed or modified by injecting killed bacteria of the species causing the diseased condition."

The advantages of using a mixed vaccine in the treatment of pneumonia is steadily gaining in favor. The following letter, taken from The Lancet (London), July 31, 1915, is a recognition of this:

"To the Editor of The Lancet:

"Sir—During the last few months I have treated four cases of pneumonia with mixed cold vaccine. Three of the patients were children. To two of these the vaccine was given on the second day of the disease, with the result that the temperature came to normal and stayed there in 24 and 36 hours respectively, though the physical signs were a week in clearing up. Even allowing for the usually shorter attacks in children, it may be fairly claimed that pneumonias of 48 and 60 hours would probably, but for the vaccine, have had a longer period of pyrexia. In the so-called abortive cases the physical signs, in my experience, clear very rapidly. The third case, injected on the third day, was a double pneumonia of the septic type. The only apparent effect was that the temperature fell from 104 to 102 degrees, reaching normal on the eighth day by lysis. The fourth case, in an adult, injected on the second day, ran a simple course with nothing of note to record. In every instance 1 c.c. of the stock mixed cold vaccine of St. Mary's Hospital was used.

"Though I have injected pneumococcus vaccine on many occasions, I cannot recall cases so striking as the first two I now record, and it may be that some pneumonias have a mixed origin and yield more readily to a mixed vaccine.

"I am, sir, yours faithfully,

"Formby, July 24th, 1915. Arthur C. Wilson."

Craig (Medical Record, Dec. 27, 1913) finds that a combined stock vaccine combined pneumococcus and streptococcus preparation serves a better purpose than a straight pneumococcus vaccine and of the results obtained says:

"As to results, they are certainly an improvement on all other methods of treatment. For we should use all other

means that we have found of benefit in conjunction with the vaccine treatment. Vaccine treatment, properly carried out, is capable only of good. Hundreds of cases have been reported with an average mortality of 5 to 10 per cent. The mortality from the old routine treatment is still 16 to 20 per cent and in alcoholic cases nearly 50 per cent in some epidemics. In twenty consecutive cases, seen by the writer in private practice, there was but one death. In hospital practice, as a rule, the cases are not seen early enough and a pneumonia is well developed before we can see them. Still last winter at Smith Infirmary, in the service of Dr. Mord, where we used it in every case, we had many remarkable cases and many recoveries where the prognosis seemed very bad. Figures are of little value unless they consist of a great many cases and the writer cannot quote enough of his own cases to sound very convincing. But I feel assured that in considerably over a hundred cases so treated I have observed that the disease runs a shorter course, the patients are less toxic, there is less fever, and generally no delirium occurs except in alcoholic cases. Convalescence also is shortened and the danger of complications is lessened. Best of all, more of the patients get well."

There are case reports where the results recorded are not so favorable, but from a close analysis of these cases it is found that the failures were due to vaccines being used too late, were given in insufficient doses at too long intervals, mixed infections were disregarded, or to a combination of these factors. The contentions of Charteris are a fair sample.

Charteris (Glasgow Medical Journal, January, 1912) contends that pneumococcus stock vaccine when given in advanced cases does not seem to alter the course of the disease and that the course of the disease was not aborted nor complication thereby avoided. An analysis of his cases shows that in only two cases was treatment started with a dosage of 20,000,000 and instead of increasing the dose as clinical symptoms indicated, the dose was decreased as low as 2,000,000. The dosage in most cases ranged from 5,000,000 to 10,000,000; no streptococcus was

employed in the stock vaccine to meet streptococcus complication.

From a careful perusal of the literature on this subject and from inquiries among my many acquaintances in the medical profession who use vaccines extensively, I have not succeeded in learning of a single case of pneumonia that died where vaccine treatment was started within twelve hours after the onset of the disease, in which the dosage was 50,000,000 or more and the dose repeated at daily intervals for three days. There no doubt are such cases, but from my experience they must be comparatively rare and must have developed under very unfavorable circumstances.

DELAYED RESOLUTION.

Where resolution is delayed there is evidence of the infection being prolonged with a probable complicating infection supervening. It is well known that pulmonary tuberculosis often has its apparent beginning with a pneumonia that does not entirely clear up. Whether the tubercle infection was dormant before the pneumonia developed, and then became active, or whether a possible tubercle infection took place after the acute symptoms of the pneumonia subsided is not known. Evidently an unresolved lung presents a favorable condition for the persistence and development of tubercle infections. There is good reason to believe that the common infectors of the respiratory tract, streptococci, staphylococci, the micrococcus catarrhalis, and possibly the Friedlander bacillus become decided complicating factors in a short time.

For this reason, when treating cases of pneumonia, where resolution is prolonged a careful bacterial examination of the sputum should be made to determine the presence of tubercle bacilli and other micro-organisms. A failure to find tubercle bacilli, especially when slight fever persists, should not exclude a tubercle infection. Where

tubercle bacilli are found, or clinical symptoms and biologic tests indicate tubercle infections, appropriate anti-tubercle treatment should be instituted. At the same time an appropriate vaccine, either an autogenous or a mixed stock preparation, should be employed to meet the existing infecting organisms.

The infection, having assumed a subacute character, inoculations should be made at four or five-day intervals. In some cases it is necessary to work up the dose to several times the size usually employed, but as a rule this is not necessary. Vaccine treatment should, however, be persistently followed out until the lung has entirely cleared up.

BRONCHO-PNEUMONIA.

The bacterial findings in broncho-pneumonia as found in repeated sputum examinations may show pneumococci, streptococci, staphylococci, micrococcus catarrhalis, influenza bacilli or other organisms to be present. It is not often that one of these organisms is found to the exclusion of the others. Usually there is a mixed infection with the pneumococcus, streptococcus and staphylococcus predominating. We find cases of typical broncho-pneumonia at all seasons of the year, but there are times when the disease is much more prevalent, spreading in epidemics.

In some of these epidemics the pneumococcus predominates, in others the streptococcus is found more frequently and in times when influenza is rife the influenza bacillus predominates. The staphylococcus is more constant, being found almost invariably. Sputum examinations in our laboratory showed a prevalence of streptococci in these cases during the winter of 1908-1909, whereas the pneumococci predominated during the winters of 1909-1910 and 1910-1911.

During 1913 and 1914 we found the Friedlander bacillus more frequently than in other years, and in quite a consid-

erable number it seemed to be the predominating factor.

L. Emmet Holt reports very extensive bacterial research in bronchial troubles in children and nurses. The results of his work show that the pneumococcus, streptococcus and staphylococcus are the organisms most frequently found, and very often they are associated.

With such a variety of pathogenic organisms found in a diseased condition it is of course impossible to know which one is the predominant or essential factor. Naturally the numerically prominent organisms would be considered the important factor, but this is not necessarily the case. The virulence of the infecting organisms must also be considered. Thus we may have staphylococcus in abundance, and not so many streptococci. In such a case the streptococcus is the greater pathogenic factor because it is a much more virulent organism. The same may be said of the pneumococcus. So in treating broncho-pneumonia with a stock vaccine it is essential to use a vaccine which is directed against the most important pathogenic organisms usually found.

During my earlier experiences in the treatment of broncho-pneumonia I used the same combined pneumococcus, streptococcus, or pneumococcus, streptococcus, staphylococcus combined vaccine, but continued experience shows that it is advisable to also include the micrococcus catarrhalis. Many doctors prefer to use a mixed vaccine that also contains the Friedlander bacillus with the other organisms mentioned.

The combined vaccine that has given the best results in my hands contains pneumococci 50,000,000, streptococci 60,000,000, staphylococci aureus and albus each 200,000,000, and micrococci catarrhalis 200,000,000 per c.c. Treatment should be started by giving 1 c.c. of this vaccine as early as possible, and daily inoculations of the same vaccine should be made the same as in lobar pneumonia for two or three

days, until improvement as shown by reduction of temperature and other favorable symptoms manifest themselves, when treatment should be continued by making inoculations at three to five-day intervals, until the patient has entirely recovered.

Dr. W. C. Wolverton (Bacterial Therapist, March, 1913) reports a number of broncho-pneumonia cases treated with a combined vaccine containing Friedlander bacillus 300,000,000, micrococcus catarrhalis 200,000,000, pneumococcus 80,000,000, streptococcus 60,000,000, staphylococcus aureus and albus each 200,000,00 per c.c., with results that are in such entire accord with my experiences that I will reprint them in toto as follows:

"Case 1. W. J. W., male, aet. 18 months. This little fellow, the writer's infant son, has from time of birth shown a marked tendency to 'take cold.' It is almost impossible to get him to take any medicine administered via the oral route, and I have failed to see any benefit to him from remedies (i. e., drugs) so given. Consequently, we have had to depend upon the bacterins almost solely in his case, and I presume that in his year-and-a-half of life I have given him at least a dozen doses of bacterin and always with immediate and most gratifying results. On Jan. 17, 1913, when my little boy was having one of his usual attacks of bronchitis, I administered a dose of a mixed bacterin; the exact components of this bacterin, and their relative proportions, I will detail a little later. Within 24 hours a decided improvement began. A week later the patient was practically well, but was given another inoculation, as a prophylactic measure, Jan. 14. Then, on Feb. 13, he was very foolishly taken on a 28-mile automobile trip, with the temperature at zero. As a result, I was awakened in the middle of the following night, to find the little one burning with fever, quick and painful respiration, harsh, dry cough, and all the other signs of beginning pneumonia. A dose of bacterin was injected into the subcutaneous tissues of the buttock; veratrine and amorphous aconitine were administered, to quickly control the pyrexia and to restore circulatory

equilibrium. Within less than 24 hours all danger was past and the boy is now perfectly well.

"Case 2. Mrs. S. A., aet. 28 years. On Jan. 17, 1913, at 11 a. m., the patient's temperature was 103 F., respiration rapid and painful, percussion dullness over lower and middle lobe of right lung, breathing-sounds diminished over same area, considerable pain in right side of chest. Here was a case of beginning lobar pneumonia. A mixed bacterin was administered; aconitine and veratrine for the fever. Same evening, 10 p. m., temperature was 100 F.; next noon, 24 hours from administration of bacterin, temperature was 99 F. Uneventful recovery followed, the patient sitting up a day or two later.

"Case 3. Baby B., aet. 9 months. Jan. 20, 1913, I was called five miles into the country to see this baby, which was just on the border-line between bronchitis and bronchopneumonia. Bacterin was administered; no other treatment except a laxative. No further visits made, as child was greatly improved next day and quickly recovered. Three older children in this family had 'colds,' and at the request of the parents I inoculated them also. The father reported that all were quite noticeably benefited by the treatment.

"Case 4. Mrs. J., aet. 36 years. Acute bronchitis; confined to bed; very troublesome cough. Was given mixed bacterin; ammonium chlorid and heroin for cough; purgative; Tr. Benzoin Co., for use by inhalation from croup-kettle. Great relief within 24 hours and unusually quick recovery.

"Case 5. Baby H., aet. 17 months. A delicate child, with acute bronchitis, which the parents thought was bronchopneumonia, and which I thought would terminate as such. Mixed stock bacterin was given; cotton-lined jacket applied; aconitine for fever; laxative. Baby was so much improved next day that no more vaccine was necessary.

"Case 6. Baby W., male, aet. 1 month. Acute bronchopneumonia: baby was almost gone before the girl-mother discovered that he was seriously ill. Mixed bacterin; cotton-lined jacket; camphorated oil and oil of eucalyptus rubbed into chest; aconitine, in exceedingly minute dosage, for

fever and to restore circulatory equilibrium. I expected this infant to die, but he was much improved within twelve hours and well in less than a week.

"Case 7. K. N., male, aet. 50 years. Had very severe attack of 'grippe' over a month before; received two doses of bacterin at that time. When seen on Jan. 25 cough had not entirely disappeared; was given a dose of bacterin to clear up the remaining bronchitis and to prevent subsequent 'colds' and possibility of pneumonia, as he was a frail-looking individual. Trouble has now disappeared.

"Case 8. Mrs. T. V., aet. 42. Acute exacerbation of chronic bronchitis. Bacterin administered Jan. 25, 1913. Also given tablets containing heroin, ammonium chlorid and squill. Patient was relieved within 24 hours, much more than by any other treatment she had ever received.

"Cases 9 and 10. Gwen and Gertie J., sisters, aet. 4 and 14 years, respectively. Children of patient in Case 4. Bronchitis; parents thought the girls had pneumonia. The mother thought so well of the results in her own case that she called me to apply same treatment to the children; this was done, and very rapid return to health followed.

"Case 11. John ——, aet. 20 years, farm-hand. Bronchitis; one dose of bacterin, with cough mixture containing heroin, ammonium chlorid, and squill, together with a purgative, saw him back at his work in a couple of days.

"Case 12. Rachel P., aet. 7 years. Lobar pneumonia, lower left lobe; well developed when first seen, on second or third day of illness. Treatment consisted of injections of bacterin, on Jan. 30 and 31, Feb. 2 and 4; heroin and ammonium chlorid for cough; inunctions of camphorated oil and oil of eucalyptus; cotton-jacket. Disease ended on seventh day, by lysis; and it ran a mild course throughout, after the beginning of bacterial therapy, each inoculation producing, always in about 24 hours, a noticeably favorable response. A microscopic examination of the sputum in this case showed that the phagocytes were crowded with pneumococci, showing the high degree of resistance developed as the result of the administration of the bacterin. The microscopic examination here showed a pure culture of the pneumococcus.

"Case 13. O. S., male, aet. 48 years. Pulmonary tuberculosis, terminal stage. The patient has received a number of doses of bacterin within the past four months, the last inoculation being on Feb. 4, 1913. After each dose the patient experiences a feeling of betterment in his general condition, which lasts for several days; the sputum becomes thin and watery and expectoration easier. Symptoms the result of mixed infection are ameliorated.

"Case 14. Jas. H., aet. 18 years. On Feb. 10, 1913, temperature 104.2, pulse 122; all the signs of first or congestive stage of lobar pneumonia present. Bacterin administered; aconitine and veratrine for fever and to re-establish circulatory equilibrium; purgative given. Next day, temperature 100.4, pulse 100; a second dose of bacterin given. On third day, pulse and temperature were normal and pneumonia had been averted.

"Case 15. Phyllis W., aet. 6 years. Severe 'cold.' Fearing the possibility of pneumonia supervening, bacterin was administered on Feb. 13, 1913. No other treatment given, but next day improvement was very noticeable and recovery took place within three days. This child was formerly extremely susceptible to 'colds,' and had two attacks of broncho-pneumonia.

"Case 16. Amos A., aet. 18 years. Bronchitis. Was given bacterin; tablets containing heroin, ammonium chlorid and squill, for cough. Reported marked improvement within 24 hours.

"Case 17. Rev. J., aet. 33 years. 'Grippe.' Was given bacterin; heroin and ammonium chlorid for cough; aspirin for the aches and pains. Temperature at 11 a. m. of Feb. 15, 1913, was 103 F.; at 8:30 p. m. it was 101.2; at 11 a. m. next day it was 98.2 F. Two days later he was driving about the country. I was called in this case, as the patient admitted, not because he thought I could 'cure the grippe,' or even relieve it very much, but because he wished me to try to ward off pneumonia.

"Case 18. Ernest H., aet. 17 years. Acute pneumonia of left lower lobe. Initial chill and rise in temperature 24 hours before. When seen at noon of Feb. 15, 1913, temperature was 104 F., pulse 118; systolic blood-pressure, 130

mm.; patient complained greatly of severe pain in left side of chest; was expectorating blood-streaked sputum. He was given 0.5 c.c. mixed bacterin; aconitine and veratrine; purgative; hot-water bottle to side. At 6 p. m. temperature was 104.6 F. At 10 p. m. patient was feeling easier, pain was somewhat relieved, and temperature was 103. Next day, at 2:30 p. m., temperature was 98.2; pulse, 70; systolic pressure, 90 mm. The change in this case was so sudden that it resembled a crisis. A second dose of bacterin was given at the time of my second visit, and a third three days later (Feb. 19, 1913), at which latter date the patient was clothed and about the house as usual. I heard yesterday that on the evening of the day following my last visit, and only six days after the onset of the disease, my 'patient' attended a 'sociable' at a schoolhouse three miles from his home.

"Case 19. Baby H., male, aet. 18 months. Broncho-pneumonia. Was given bacterin and minute doses of aconitine. Improvement was manifest in 24 hours. On Feb. 19, four days after the first visit, a second dose of bacterin was administered and I have not seen the child since, but understand that he is rapidly recovering.

"Case 20. Baby A., female, aet. 18 months. I saw this case yesterday for the first time. She had had a 'cold' for some time, and the mother had been treating it with 'Pinex.' Yesterday morning the child began vomiting, and I was summoned. Gastric lavage was used; a dose of bacterin given for the bronchitis; all feeding stopped. A sister of the baby was just in my office to tell me that the baby is greatly improved today.

"Cases 21 and 22. The father of the last patient, when the rationale of bacterin therapy was briefly explained to him, said that he thought I might just as well try it on him and a daughter, both of whom had been suffering from coughs for some time. I did as he wished, and understand that both patients are improved today. I am sure the girl who was just in the office was much better.

"Case 23. I cannot refrain from reporting just one more case which just came to mind, and as this is 'No. 23' it will have to be the last. About three months ago I was called into the country to see an old Norwegian lady who is in her

94th year. She had long been a sufferer from chronic bronchitis. At the time I first saw her a broncho-pneumonia had developed. I gave her four doses of bacterin during a period of about ten days. No, she did not die; she recovered from her broncho-pneumonia and is still living. * * *

"Since beginning the use of the bacterins in pulmonary diseases the writer has lost only one case of pneumonia, and that was an infant of 2 months. I feel that even this one might have been saved had the parents called me early enough."

As broncho-pneumonia is a disease which is particularly prevalent among infants and children, the mode of administering vaccine is of special advantage. A hypodermic injection insures one at least that the patient has the required dose and the mother and nurse are relieved of the unpleasant need of giving the baby medicine. The dose of the vaccine being small (from ¼ to ½ a cubic centimeter), it often can be injected before the baby is aware of what has happened. Usually only two or three doses are required in these cases to effect a cure.

PLEURISY.

Pleurisy is one of those painful inflammatory processes in which a diagnosis can usually be made from the clinical symptoms. I have had frequent occasion to make bacterial examinations of pleuritic fluid following acute pleurisy, but in most cases have found the fluid sterile. From this it should not be inferred, however, that pleurisy is not of bacterial origin. The pneumococcus is the most constant organism in these cases. Where there is much pleuritic effusion it is always advisable to aspirate. If the vaccine treatment is started early the inflammatory process will be in many cases promptly aborted with a resulting relief from pain and the production of a very limited amount of pleuritic fluid. I have seen relief from pain follow twelve hours after an inoculation of vaccine. While the pneumococcus

is the principal infecting organism in these cases yet as a routine treatment I think a pneumo-strepto staphylococcus combination vaccine answers the purpose better because of the possibility that staphylococci and streptococci may also be present.

Chronic pleuritic adhesions with recurrent pleurisy may be very satisfactorily treated with suitable bacterial suspensions. The combination of micro-organisms that should be selected is the same as that used in pneumonia—streptococcus and pneumococcus and, occasionally, streptococcus, staphylococcus and pneumococcus.

The treatment usually requires a longer time and more persistence, just as experience will show it to be necessary in the treatment of other chronic infections. It must be borne in mind that other treatment, both local and general, is not contraindicated when vaccines are used.

The frequent association of tubercle infection with pleurisy makes it necessary to determine the presence of tuberculosis when a case of pleurisy is under treatment.

EMPYEMA.

When the pleuritic fluid becomes actively infected we have an empyema requiring surgical procedure to evacuate the pleural cavity. The usual procedure is to resect a rib so as to give sufficient drainage until the pleural cavity has healed. With the use of vaccine it is not necessary to make a rib resection in cases where the diagnosis is made early. An incision between the ribs with two drainage tubes will suffice.

Bacterial examination in these cases shows the pneumococcus as the principal organism, streptococci, staphylococci, and colon bacilli are also found. After using vaccines in these cases the pus becomes very thin within a few days and then develops the appearance of serum. When the

purulent character of the discharge has subsided and a serum has taken its place, the drainage tubes may be removed and the wound allowed to close. In one case of empyema following a severe attack of pleuro-pneumonia in a child 5 years old, I withdrew the tubes on the fifth day. The wound healed without any subsequent trouble.

Since the infection is often of a mixed character, a combined vaccine of pneumococcus 40,000,000, streptococcus 30,000,000, staphylococcus aureus and albus each 100,000,000, is given to best advantage. Inoculations should be repeated at two or three-day intervals until the inflammatory process subsides.

In chronic cases that have been draining for a long time a large variety of organisms are often found. Bacillus pyocyaneus infections are not common. In all probability this organism is in most cases a secondary invader. Bacillus proteus, colon bacilli and saprophytes are also found. The results in these cases of long standing are not so uniformly good. In some cases autogenous vaccines will give results where stocks have failed, and in others stocks serve a better purpose. Not infrequently, however, indifferent results are obtained.

PULMONARY ABSCESSES.

It is not necessary to enter here into a detailed description concerning pulmonary abscesses and their development. As a means for proper vaccine treatment it is well to take into account the three principal conditions under which pulmonary abscesses develop: intense localized infection, pulmonary embolism and extension of an abscess through the diaphragm from the abdominal viscera.

Where pus accumulation exists, drainage is the first essential, but to build up an immunizing resistance to limit the ravages of the localized infection is of equal importance. When the abscess is confined to the lung, the same infect-

ing organisms usually found in respiratory infections are responsible and demand the same vaccine that is employed in empyema or broncho-pneumonia.

In cases where the abscess extends from an appendicitis, or from some other abdominal organ, the colon bacillus is almost invariably the principal offender and should be included in the vaccine.

If the abscess has broken into the bronchi and discharges, a bacterial examination of the pus will reveal the character of the infection and in this way aid in determining the source of the abscess, while at the same time it will indicate what vaccine should be employed. Where the drainage through the bronchi is adequate the use of vaccines will naturally aid in bringing about a recovery.

ACUTE BRONCHITIS.

Bronchitis, as was to be expected, is caused by the same varieties of microorganisms as those responsible for infections of the nose and throat. The pneumococcus, streptococcus, micrococcus catarrhalis, and staphylococcus are the most constant and persistently pathogenic. During influenza epidemics the influenza bacillus is found in a large majority of cases; otherwise is not so frequently present. The Friedlander bacillus is also frequently found and, when present, imparts a characteristic disagreeable odor to the breath and a distinct tendency to chronicity, where immunization is not employed. The colon bacillus is also occasionally found and when present causes the foul fetor of the breath characteristic of the gases produced by this organism. The bacillus pyocyaneus is a complicating factor in a small percentage of cases. The pseudo-diphtheria bacillus is present in a fair percentage of cases, but does not appear to be particularly pathogenic.

A bronchial infection may start primarily in the bronchi or may extend downward from the larynx or throat. Some-

times the bronchial infection starts simultaneously with a rhinitis or pharyngitis. In the early acute stages it is very important to initiate vaccine treatment at once because there is always great danger of a broncho-pneumonia developing. This is particularly the case with infants.

Early treatment being important, a small dose of stock vaccine should be employed containing the principal infecting organisms, namely, for an adult, pneumocci 30,000,000, streptococci 20,000,000, staphylococci 80,000,000, micorcocci catarrbalis 80,000,000. A slightly larger dose three days thereafter. By this time all the acute symtoms of the disease should be relieved. When influenza bacillus infections are prevalent, 60,000,000 influenza bacilli should be included in the vaccine. To insure against a relapse, two or three more slightly larger inoculations of the same vaccine should be given in five to seven-day intervals.

Many physicians prefer to use as a routine a vaccine also containing the Friedlander bacillus, because this organism is frequently found. The only disadvantage in using this combination as a routine is that the Friedlander vaccine often causes more local reaction, and if no Friedlander bacillus infection is present this soreness at the site of the injection, while transient, is needless. Otherwise the therapeutic results are just as good and, of course, when a Friedlander bacillus infection is present this combination should be employed.

The fact that some drugs will relieve irritating coughs has brought them into general use. When treating bronchitis with vaccines, bronchial irritation is, as a rule, so relieved that palliative measures are not often necessary; but occasionally we have cases in which the mucous in the larger bronchial tubes, while scanty, becomes very tenacious and difficult of expulsion. In these cases the usual expectorants are of great value in giving relief during this stage of the infection.

The advantages obtained by treating infants and children with vaccines in acute bronchitis, as in other acute respiratory infections, can hardly be overestimated, not only from a therapeutic standpoint, but from that of convenience of application as well. The average dose of a vaccine for an infant or small child is from two to five minims. If the little patient is laid on his stomach across the nurse's knees, a sharp hypodermic needle can be inserted into the exposed buttocks, the few drops of vaccine injected, and the needle withdrawn before the patient is aware of what has happened. I have frequently given vaccines to infants in this way without a murmur from the little patient. This will be ample treatment for the next 24 hours. The nurse and mother are relieved from the disagreeable task of giving the baby medicines, frequently of indifferent value, that it does not want, and often will not take, no matter how pleasantly and carefully it has been prepared. When the mother sees how much better the baby is the next day and that "the treatment is so easy," no objection will be raised if it is necessary to repeat the inoculation.

CHRONIC BRONCHITIS.

Chronic bronchitis is caused by the same organisms that are found in the acute conditions of this disease. In the treatment of these cases, however, it is very important to make microscopic examinations of the sputum to determine the presence of a tubercle infection. Many a case of a pulmonary tuberculosis has been allowed to progress without instituting appropriate treatment for tubercular infections, because the cough was considered "an ordinary bronchitis" until the disease had developed beyond control. When no tubercle bacilli are found in the sputum, clinical symptoms for a possible tubercle infection should be carefully observed. In addition to stethoscopic examinations, a Von Pirquet cutaneous tuberculin test, or an X-ray examin-

ation should be made. When tuberculosis is excluded most cases are found to be mixed infections by pneumococci, streptococci, micrococci catarrhalis and staphylococci. For this reason a combined vaccine containing these organisms may be employed as a routine treatment, but where prompt relief does not take place after two or three inoculations a careful bacterial examination, by cultural and microscopic methods, should be made to determine the presence of other infecting organisms, when a stock vaccine corresponding to the organisms found or an autogenous vaccine for unusual species of bacterin should be employed.

When collecting sputum for bacterial examination or culture purposes, care should be taken to avoid contaminating the sputum with saliva as much as possible. This is best done early in the morning. During the night considerable sputum accumulates which rises freely in the morning. Before collecting the specimen the mouth should be thoroughly cleaned and then, by forcible coughing, the sputum may be expelled direct into a receptacle previously sterilized by boiling, without allowing the sputum to remain in the mouth long enough to become extensively mixed with saliva. When making cultures and slides a clump of sputum should be selected and washed with sterile water, then the clump separated and some portions from the inside of the clump taken for culture inoculations and smears on slides.

Chronic bronchitis is one of the chronic infections in which vaccine inoculations are very efficient therapeutic agents. This may be accounted for on the ground that the lung tissues have a very free blood supply which allows a liberal amount of immunizing substances contained in the blood to reach the infected area. Cases that have resisted every other treatment will often make complete recoveries in a comparatively short space of time. The following history reported by Dr. McColl (Bacterial Ther-

apist, February, 1914) shows what can be accomplished in an extremely bad case:

"A woman 68 years old had been sick for five months with extensive bronchitis and was steadily growing worse. Repeated sputum examinations showed no tubercle bacilli. She had been treated by several physicians, among them the late lung specialist, Dr. Shurley. She was emaciated to a skeleton and was obliged to remain in a reclining position day and night. She could take no solid food and sustained herself by taking malted milk in teaspoonful doses. She was so nearly dead many times that I did not expect to see her alive at my next call, and often wished she would die to relieve the agony. I was called to see her during all hours of the night and averaged three calls a day for several months. No hopes for her ultimate recovery were entertained by her husband; to give a measure of relief while life lasted was all that was hoped for. To use a new remedy in a case like this was certainly justified. She began to improve after the first dose of vaccine, her cough became less irritating and she was able to take more nourishment. It was not long before her appetite and digestive capacity became such that she could eat anything. Inoculations were made at five-day intervals at first and one week apart later on. After three months' vaccine treatment her cough had disappeared and her general health was restored. It is now over four years since her illness and she is still enjoying perfect health. She is well nourished, with a liberal amount of fat on her body, and is actively employed doing housework every day."

When the bronchitis is of very long standing and the bronchial tubes have become stretched from excessive coughing, it is not to be expected that normal conditions can be restored. But even in such cases the immunizing influence of the vaccine will relieve the irritation and diminish the amount of mucous formation, when the cough will become of minor significance.

These chronic bronchial infections have a tendency to reinfection during a prevalence of colds, and for a time one is led to think that vaccine treatment has failed in so

far that it has not prevented these new attacks. A little closer observation, however, will show that these acute relapses are of comparative short duration; when they do take place, vaccines should be given at short intervals, one or two days apart, for two or three inoculations, and after the acute symptoms have subsided, four to seven days apart. By persistently continuing the treatment, most obstinate cases are cured. My experience with the use of vaccines in bronchitis has been sufficiently extensive to warrant quite positive conclusions. Inasmuch as my conclusions conform so closely to Allen's experiences I will take the liberty of quoting from his book, "Vaccine Therapy and Opsonic Therapy," fourth edition, p. 361:

"Personally, I have never seen the case, excluding one or two of advanced emphysema, which did not benefit, speedily and markedly, from the administration of the suitable vaccine in suitable dosages at suitable intervals, and I do not believe that such a case exists. The duration of the attack is reduced, convalescence is shortened, complications obviated, and relapses reduced to a minimum. In many cases the judicious use of immunizing doses at appropriate times of the year will do much to prevent the patient falling victim to fresh infection."

Treatment should be started with a small initial dose, because some of these chronic cases are liable to have marked reactions at the point of injection unless this precaution is observed. During the first day a slight focal reaction, as indicated by a little more cough and increased expectoration, may take place, but this will soon subside with signs of marked improvement. The initial dose of the various organisms should be about as follows: Pneumococci 30,000,000, streptococci 20,000,000, micrococci catarrhalis 80,000,000, staphylococci 100,000,000, Friedlander bacilli 100,000,000, influenza bacilli 100,000,000, and colon bacilli 80,000,000. Various combinations of these organisms to conform with the existing infection should be employed, but pneumococci and streptococci should be in-

cluded in a combined vaccine even where no corresponding organisms are found in the sputum, because infections by the pneumococcus or streptococcus are very liable to become complicating factors in the presence of other infecting organisms.

When an autogenous vaccine is employed where only one or two organisms appear to be the cause, frequent culturing of the sputum to determine the entrance of a possible new infecting bacteria is necessary.

The dose should be increased as indicated by the amount of reaction, both at the point of inoculation and constitutional. When reactions at the site of inoculation are slight the dose may be increased to three or four times the initial dose within three or four inoculations, but if reactions are more marked the dose should not be so rapidly increased; and if rather severe reactions take place it is not wise to materially increase the dose until a tolerance to the vaccine has developed. In some exceptional cases it is necessary to work up the dose to ten or fifteen times the size of the usual initial dose, before the infection can be eliminated. When large doses are resorted to it is as a rule advisable to make inoculations at seven to ten-day intervals.

The question of prophylactic inoculations to prevent these bronchial infections during the prevalence of colds is a very important one. Immunization to the various micro-organisms responsible for these colds is not of a permanent nature, but experience indicates that an immunity from vaccine inoculations is of greater duration than from spontaneous recovery from the infection in these cases. In patients that are prone to "catch colds," immunity is liable to wear off in the course of three or four months, and this is especially true where the vaccines have been used only for a short time. For this reason it is of advantage to give two or three inoculations at weekly intervals

every three or four months and in this way ward off these periodical attacks.

ASTHMA.

Asthma is now definitely classed as due to infection. The association of asthma with chronic bronchitis would naturally lead one to suspect an etiologic connection, but some cases of severe asthma exist without an accompanying bronchitis. This might lead one to think that frequent bronchial infections in asthmatics is merely a coincidence, but a closer analysis shows that the focus of infection which is responsible for the spasmodic contraction of the small bronchi may be in a remote part of the body.

Dr. R. H. Babcock (Journal of the Amer. Med. Asso., June 26, 1915), in a critical analysis of the etiologic relations of asthma to infection, considers asthma an anaphylaxis due to absorption of bacterial proteins from some focus of infection. He finds that while this focus of infection is most frequently located in the lower respiratory tract, it may be in the gallbladder, sinuses, nose or some other part of the body. He describes in detail the relationship of protein sensitization to anaphylaxis and asthma. He considers immunization by means of autogenous vaccine for the purpose of eliminating the focal infection the most logical treatment, and from experience with this method finds that permanent cures may be secured even in cases where the disease has been of long standing. When the focus of infection involves a localized pus accumulation, interference to establish drainage is recommended, and where possible the focal infection should receive local treatment with the object in view of eliminating the infection in conjunction with the use of vaccines.

When the focal infection is located in the respiratory tract the same infecting organisms that cause nose, throat, and bronchial infection are responsible for the asthma. When the responsible focus of infection is located in the

abdominal viscera a vaccine corresponding to the organisms usually causing infections in these organs should be employed.

My experience with the use of both stock and autogenous vaccine in the treatment of asthma has been quite extensive, especially so in cases where asthma was associated with bronchitis, and the results have been so pronounced that there can be no question in my mind as to the therapeutic value of the vaccine treatment of this disease. In making a diagnosis, a possible tubercle infection should not be overlooked. Where prompt improvement does not take place after a few vaccine inoculations, careful cultural and microscopic examinations should be made to determine the bacterial flora causing the infection in the case under treatment. From the nature of the disease we should not expect as complete recoveries in cases of long standing as can be effected by the use of vaccines in acute bronchitis. In asthma, the spasmodic contractions of the bronchial tubes prevent the aircells from fully expelling the inhaled air, and from repeated dilations over a long period of time the aircells become enlarged, stretched. Where excessive mucous from a bronchial infection exists this obstruction to a free air passage is aggravated and naturally the aircells suffer more. An extensive emphysematous condition necessarily will not allow as complete restoration of the respiratory function as where no stretching of the aircells has taken place, but when the excessive mucous from the infected bronchi and the spasmodic contraction of the bronchial tubes is eliminated through the immunizing influence of the vaccines it is remarkable to what extent these abnormal conditions will be remedied.

I have repeatedly taken cases of chronic asthma and restored them to health and usefulness after they had been unsuccessfully treated with drugs and by other methods for years. Improvement generally takes place soon after treat-

ment is started and often entire relief is obtained from four or five inoculations, but if treatment is not continued by inoculations at weekly intervals for several months, relapses are liable to take place. These relapses are in all probability reinfections. When these reinfections do take place it is necessary to give vaccines at two or three-day intervals for several inoculations and when the acute symptoms of the infection have subsided inoculations should again be given at four to seven-day intervals. These cases are often discouraging, but if persistently followed up success will eventually be attained. I have treated cases where inoculations were made at somewhat regular intervals for a year or more before fairly permanent relief was obtained, and even then slight attacks would follow on "taking colds." A large majority of asthmatics, however, respond more favorably to the vaccine treatment. The following case will serve as an illustration: Mr. E. W., aged 48, proprietor of a hotel, called at my office July 15, 1913. Has had asthma since he was a small boy. Attacks were most severe when "taking colds," but at times he was entirely free from the disease. The asthma steadily grew worse and during the past fifteen years he has been a continuous sufferer. Chest examination revealed extensive mucous rales all over both lungs, with the characteristic wheezing of chronic asthmatics. Slight exertion would cause fatigue and labored breathing. Treatment was started by giving 0.3 c.c. of a mixed stock vaccine containing streptococci 60,000,000, pneumococci 80,000,000, micrococci catarrhalis 200,000,000, Friedlander bacilli 300,000,000, staphylococci aureus and albus, each, 200,000,000 per cubic centimeter. Inoculations were repeated at four-day intervals for the first three inoculations and at weekly intervals after that, the dose being gradually increased to one cubic centimeter. Improvement was observed after the third inoculation, in that he could breathe more freely and coughed less. He continued to improve and by October was entirely free from his asthma

and bronchitis. The same vaccine treatment was continued for six weeks more, when he felt so well that he considered further treatment unnecessary. In March, 1914, he took a bad cold, with a resulting bronchitis and a return of the asthma. He called at my office rather discouraged. The same vaccine was given again and after twelve more inoculations he was entirely free from his bronchitis and asthma. He has had no asthma since, and feels entirely well at the present time, although he had a cold during August, 1915, which cleared up without any treatment.

The following case reports by Dr. M. McColl (Bacterial Therapist, February, 1914) will also be of interest:

"Mrs. Fred G., aged 54 years. Suffered eleven years with bronchial asthma. She was treated by six doctors of Port Huron, Mich., covering a period of nine years, with no results. Her case was so hopeless that several times they reported her as dying. Their opinion was that the only chance she had was to move from Michigan. For nine years she was not able to lie down in bed and was obliged to sleep in reclining position. The mucous expectoration was so copious that she would have a choking sensation when lying down. Vaccine treatment was started with a stock vaccine containing Friedlander bacillus 300,000,000, micrococcus catarrhalis 200,000,000, pneumococcus 80,000,000, streptococcus 60,000,000, staphylococcus albus and aureus, each 200,000,000, of which she received 26 inoculations, at first every four days until improvement took place, then once a week. Last treatment was given in August, 1913. Since then she has been in splendid condition as regards the asthma and bronchial condition as well. A little bronchitis still remains, but does not distress her. I have not been called to see her since then for any other trouble. She has gained in weight and flesh, and is able to do housework without any difficulty. Before starting treatment with the vaccine she was so enfeebled that she could scarcely walk. With the exception of neuritis, that bothers her at times in the left arm, she is a well woman."

The following is an illustrative case reported by D. H. Anthony, M. D. (Bacterial Therapist, July, 1915):

"The patient in question is a woman 47 years of age, in the climacteric period. She is married and has a daughter 16 years old. Up to five years ago this lady enjoyed good health, but then suffered an attack of bronchial pneumonia, which left her with a predisposition to bronchial asthma, which seized her at certain periods, rendering her breathing most difficult. She was susceptible to taking cold and would suffer from asthma and bronchitis in climatic changes. She was treated by the local physicians off and on for the past five years. I was called to see her for the first time last September and found her suffering from extreme difficulty in breathing, due to the fact that the tubes were clogged.

"Last February she took cold and suffered a very severe attack. My usual medicinal remedies proved fruitless, and she was far from improving, so I decided to use vaccines. On March 14th I injected 5 minims of stock vaccine containing Friedlander bacilli 300,000,000, micrococci catarrhalis 200,000,000, pneumococci 80,000,000, streptococci 60,000,000, staphylococci py aureus and albus, each 200,000,000 per cubic centimeter.

"She had a severe reaction twelve hours later and, calling upon her the next day, I found her slightly improved.

"On March 18th I gave her 5 minims more and I was gratified with result.

"March 23, 10 minims. The next day I found her sitting up; she remarked that she felt so much better.

"March 27th she felt so well that she walked to my office for treatment. I injected ½ c.c. on this occasion and she told me she was experiencing her first real sleep at night, being free from the difficulty in breathing.

"April 2nd I injected ½ c.c. April 7th I injected ½ c.c. Continues to feel improved.

"April 10th I injected ½ c.c. April 14th I injected ¾ c.c. April 22nd I injected 1 c.c. April 29th I injected 1 c.c. May 17th I injected 1 c.c. Continues to feel well. Cough all gone. She is gaining in weight and the attacks of vertigo of which she complained have disappeared.

"May 24th I injected 1 c.c. June 2nd I injected 1 c.c. June 11th I injected 1 c.c. Her susceptibility to colds has disappeared.

"The results in this case have been very gratifying. She is still under my care, but I feel very enthusiastic over vaccine therapy, as this was one of the worst cases of chronic bronchial asthma I have ever come in contact with."

When we consider the inadequacy of conventional remedies in the treatment of asthma it is no wonder that most of these sufferers have given up hope of ever getting better. Some time ago a young woman called at my office and said: "Doctor, if I can't get rid of this asthma, I want to die." She had been suffering for twelve years and during most of this time had been under the care of a physician who was a near relative and of the various consultants he advised. She had been under the vaccine treatment for three months and is much improved, with good prospects of an ultimate complete recovery.

On account of the unsatisfactory results from the usual methods of treatment the large majority of asthmatics go through the greater part of life without medical attendance. If vaccines were regularly employed in the treatment of asthma by the medical profession it would not be long before the victims of this disease would become aware that something can be done for them, and then they would apply for treatment, instead of going along neglected.

WHOOPING COUGH.

That the Bordet-Gengou bacillus is the cause of whooping cough is now generally admitted. This has been thoroughly demonstrated by the results attained in the treatment of the disease with a vaccine prepared from this bacillus.

To attain the best results early treatment is necessary. This necessitates an early diagnosis. Friedlander (Journal

A. M. A., March 28, 1914; American Journal of Diseases of Children, August, 1914; The Lancet-Clinic, Jan. 2, 1915) did some extensive work with the complement deviation method to determine the early presence of the infection before the paroxysmal stage develops. The isolation of the organism from the bronchial secretion involves considerable difficulty because the organism is a poor grower on culture media, and other organisms which are always present have a tendency to overgrow the Bordet bacillus. Furthermore, this organism may be confused with the influenza bacillus by one not thoroughly familiar with laboratory work. Friedlander always found a positive complement deviation in cases of whooping cough during the paroxysmal stage and never had a positive reaction where no whooping cough was present. He also found that a positive reaction was acquired during the early catarrhal stages and considers this method as a practical means of making a positive early diagnosis. He employed the Noguchi hemolytic system and used only fresh, active serum and fresh, active antigen, making a standard emulsion of live washed bacteria for each test.

It took some time to recognize the effectiveness of the vaccine in whooping cough, because in the beginning insufficient dosage was employed; because the prevalence of mixed infections as a means of prolonging the disease was not sufficiently taken into account; and last but not least, because prominent pediatrists, while they conceded the logic of prophylactic inoculations of Bordet bacillus vaccines to prevent whooping cough in exposed children, refused to recognize the soundness of using the vaccine for therapeutic purposes. They made the theoretical objection that the existing infection induced sufficient antigenic activity to arouse a maximum amount of antibody production, and that there was no scientific reason why vaccine inoculations should hasten immunization in an acute infection of this

character. This thought was clearly brought out during a conversation with a prominent pediatrist in New York City a little over a year ago. He had not employed pertussis vaccine in the treatment of whooping cough, and was only interested in its prophylactic application because it appealed to him, but he had not even given the latter a trial.

To make certain of the therapeutic value of pertussis vaccine, it is important that it should be given early in the course of the disease, in sufficiently large doses and at not too long intervals, and to give a vaccine in which the other bacteria are represented. Upon positive diagnosis during the catarrhal stage by means of the complement deviation test and starting treatment early it is easy to positively determine the therapeutic advantages of pertussis vaccine inoculations for therapeutic purposes. If by this means the paroxysmal stage of the disease is almost or entirely avoided, the therapeutic value of the treatment is clear. Friedlander (The Lancet-Clinic, Jan. 2, 1915) says:

"But it is not merely in the direction of early diagnosis that the test is of value. As is well known, the vaccine treatment of pertussis is now under trial, and many independent observers are testing this method of treatment. Unfortunately, the diagnosis is ordinarily not definitely made until the paroxysmal stage is reached. It is a rule of all vaccine therapy that its success is in direct proportion to the time of its administration. The earlier the vaccine can be given in any infection, the better the results following its use.

"Using the complement deviation test as a guide, we have been commencing our vaccine treatment of pertussis in the catarrhal stage. Thus given, vaccine therapy has yielded us very gratifying results. Personally, I am convinced that the dosage of vaccine, as ordinarily administered, is far too small, and at my request Dr. G. H. Sherman, of Detroit, has prepared a vaccine of the Bordet-Gengou bacillus of double the ordinary strength. The cases under treatment with this new vaccine have responded remarkably well."

The suspension that was prepared for Dr. Friedlander contained 400,000,000 Bordet bacilli per cubic centimeter, and that is now being extensively employed as a standard suspension in our laboratory.

When the whooping cough has advanced to the paroxysmal stage complicating infecting organisms are practically always important factors. Of these the pneumococcus, streptococcus, micrococcus catarrhalis, and, in the presence of influenza epidemics, influenza bacilli, are the most constant. For this reason in advanced cases of pertussis a mixed vaccine is preferably employed. A combined vaccine containing Bordet bacillus 400,000,000, micrococcus catarrhalis 100,000,000, pneumococcus 40,000,000, streptococcus 30,000,000 per cubic centimeter, serves well. When the influenza bacillus is present, 100,000,000 of this organism should be added. Infants should receive somewhat smaller doses than children, but infants tolerate vaccine inoculations well, severe reactions being seldom observed. For children from 4 to 6 years of age the initial dose of the above vaccine should be about 0.3 c.c. Inoculations should be made at three or four-day intervals and the dose gradually increased to 1 c.c. within three or four inoculations. In infants the initial dose should be 0.2 c.c. When a broncho-pneumonia complicates a whooping cough, inoculations should be made at daily intervals for several days until the acute pneumonic symptoms have subsided and then three or four days apart. After the paroxysmal cough has subsided it is advisable to give the vaccine at weekly intervals for three or four weeks to insure against a relapse. On two occasions I have seen such relapses where the vaccine treatment was discontinued after the cough had been relieved.

For prophylactic purposes a Bordet bacillus vaccine containing 400,000,000 organisms per c.c. is advantageously employed. The first dose should be 100,000,000, the second

dose 200,000,000, and the third dose 400,000,000. Inoculations should be made at five to seven-day intervals.

In whooping cough acquired immunity usually lasts through life. How long an immunity from vaccine inoculations will last has not been determined, but judging from the results obtained in typhoid and meningococcus prophylaxis, there is good reason to believe that an immunity from prophylactic inoculations of pertussis vaccine will also continue long enough to be of substantial value.

Freeman has used this vaccine extensively, giving 25,000,000 dead organisms to a dose, and finds that the length and severity of the disease is reduced to about one-half the usual course. Allen ("Vaccine Therapy," p. 266) thinks he has obtained better results by giving 50,000,000 or 100,000,000 to a dose.

Extracts From General Literature.

Dr. Edwin E. Graham (American Journal of Diseases of Children, January, 1912, p. 41) reports 24 cases treated in private practice with whooping cough bacillus vaccine. In his first cases doses of 20,000,000 bacilli were employed with no untoward effects. The dose was increased to 40,000,000. From all indications the vaccine seems to be non-toxic. His results were certainly encouraging because the benefit of the vaccine treatment was not only observed by the doctor but by the nurses, and other members of the family as well.

An interesting communication entitled "Pertussis Vaccine as a Curative and Prophylactic Agent," by Drs. Saunders, Johnson, White and Zahorsky, which was read before the St. Louis Pediatric Society, was published in the March, 1912, issue of Pediatrics. These gentlemen have used a vaccine prepared from Bordet's bacillus in 40 cases of whooping cough, some in private practice, and a number at the Episcopal Orphanage and Bethesda Hospital during a recent epidemic.

They have observed no ill effects from its use and procured benefit in all cases in which the cough was not of more than two or three weeks' duration, and in some of longer standing. The improvement in number and severity of paroxysms was often evident in less than 24 hours, showing no evidence of a negative phase.

The conclusions of these authors are as follows:

1. "As a prophylactic agent we have no hesitation in recommending the pertussis vaccine. Whilst it is true that any infection will postpone or interrupt the course of pertussis, this agent alone will absolutely prevent it. The immunity is of uncertain duration, but the injections may be repeated, and it is of the utmost importance to postpone the disease until the first two years of life are passed. The failures reported by other observers must be attributed to an impotent vaccine or an insufficient dosage.

2. "As a remedial agent, success depends upon the promptness of administration and the freedom of the patient from complications at the time.

3. "In no case should other treatment be withheld if indicated, especially in infants, who may be spared convulsions or bronchopneumonia by the use of emetics, sedatives and some member of the aromatic group. It is quite possible that much better results may be obtained in late cases by the use of larger doses.

4. "In view of the high mortality from pertussis in young children, there should be a systematic effort made to determine the duration of artificial immunity and to keep them protected."

Wilson (New York Medical Journal, May 10, 1913) reports 24 cases treated successfully with pertussis vaccine in doses ranging from 20,000,000 to 40,000,000. The shortest duration of the disease was 9 days and the longest 48, averaging 23 days.

Sill (American Medicine, June, 1913), in concluding, says that he is fully convinced that from his past experience pertussis vaccine is the best means at our command in

treating whooping cough and that it not only alleviates symptoms and cures quickly, but in a measure also prevents complications which so often prove fatal.

Dr. W. C. Wolverton (The American Journal of Clinical Medicine, August, 1914), after giving a number of case reports, concludes:

"1. In my own personal experience, in a limited number of cases (36), the results of vaccine therapy of whooping cough have been very satisfactory indeed.

"2. In no case occurring in my own practice has there been any unpleasant symptom resulting from the vaccine treatment, nor can I learn of any such from a perusal of the literature.

"3. Experience seems to prove that the best results are attained where large doses (50,000,000 to 200,000,000 killed bacilli) of the vaccine are employed. The fear of a harmful negative phase, here as elsewhere in the field of bacterial therapy, apparently has been greatly overdrawn. I have used only large doses and have never seen any harmful effect whatever. Where failures have been reported, invariably too small doses of the vaccine have been used.

"4. As a prophylactic and in early, uncomplicated cases of pertussis, the plain Bordet bacillus vaccine suffices. But in late cases or in cases complicated with bronchopneumonia, a mixed vaccine containing the pneumococcus, streptococcus, and micrococcus catarrhalis, in addition to the Bordet bacillus, is indicated.

"5. The Bordet bacillus vaccine is a dependable prophylactic, if used promptly after exposure, or before exposure when an epidemic is known to exist. My own two children, aged 2½ and 7 years respectively, have repeatedly been exposed to bad cases of whooping cough during the past two months. After their first exposure each was given 100,000,000 killed bacilli; this dose was doubled a week later, and again in two weeks. Neither child has since contracted the disease.

"6. I believe, from my experience, that the gluteal region is the most likely spot into which to inject this or

any other kind of vaccine, in the case of children. There is here plenty of loose subcutaneous tissue into which the vaccine can easily be injected, without causing undue pain and inconvenience. A further advantage is that the child cannot see what you are about to do, when it is turned face downward across its mother's lap.

"7. An honest trial will convince the most skeptical that in the vaccine therapy of whooping cough we at least have made a wonderful advance over the old-time empirical remedies (so-called)."

Dr. Paul Luttinger (New York Medical Journal, April 24, 1915) said that at the whooping cough clinic, treatment was started with doses of 250,000,000. Results depended upon the size of the dose. In referring to Dr. Hartshon's statement that he had abandoned the use of vaccines in whooping cough he said that if the doctor would give larger doses he might get better results. He maintained that vaccine treatment gave better results than drug treatment.

Dr. Paul Luttinger (New York Medical Journal, May 22, 1915, p. 1043), as a result of work done in the treatment and prophylaxis in whooping cough by the Research Laboratory of the Department of Health of the City of New York, concludes as follows:

"1. Pertussis stock vaccines as prepared by the Bureau of Laboratories seem to have a prophylactic value when given in high doses.

"2. In the treatment of pertussis these vaccines seem to have shortened the duration and severity of the paroxysmal stage; the average duration of the whoop being 25 days, compared to 40 days of those treated with drugs.

"3. Further experiments with the view of obtaining more effective vaccines and a closer co-operation of the profession in public health education may help in the eradication of pertussis, this scourge of childhood which kills yearly 10,000 American children."

Dr. Ward Bryant Hoag of New York City (American Medicine, April, 1916) has contributed a valuable paper

with report of cases treated at St. Mary's. He attributes indifferent results obtained by early observers to insufficient dosage and possible inefficient vaccine. Concerning dosage and results he says:

"Any remedy which will shorten the paroxysmal stage of pertussis one week, or longer even, should be hailed as a boon, for it is during the latter weeks, when the patient is increasingly weakened by stress, deficient nutrition and want of sleep, that the greatest possibilities of complications and sequelae arise.

"In a number of cases two and a half and three billion organisms have been given in one injection to children under five years of age, with only benefit apparent. To date we have had practically no complaint of reaction, and no soreness of arm where injection was given. Two patients were attended by trained nurses and temperatures taken regularly. On neither occasion was there a particle of febrile reaction following the vaccine.

"Painting the arm in the region of the deltoid insertion, with tincture of iodine, and placing the syringe in 95% alcohol after each injection, have been the antisepsis observed. The injections have been made subcutaneously.

"Our youngest patient was 22 days old, with a spasmodic cough so severe that respiration was practically suspended with each paroxysm; at the time of the first injection of one half c.c. of vaccine he had been coughing 'about one week.' He recieved 4½ c.c. all told. First injection was Aug. 16th, and last Sept. 3rd, when he was practically well. Sept. 20th was reported in fine condition. The eldest patient was 26 years old, a trained nurse. After a severe cough of ten days duration, Sept. 14th she received her first injection. Whooping began on the 17th. Received last injection, Oct. 6, nineteen days after the whoop began. Slept all night after the 28th of Sept., eleven days after the beginning of the whoop. All told received 18 c.c. of vaccine. On Sept. 25 and 28, she received 3 billion each injection and complained of feeling sick the next morning, but she 'slept well all night' after each injection.

"This patient feels, without a particle of question, that the vaccine, which was her only medication, gave her the greatest possible relief, lessening the severity and frequency of the paroxysms, and particularly affording her such a sedative effect that she got a good night's sleep almost from the time of the first injection. Before the vaccine was begun she got hardly any sleep.

"We have felt the earlier the patients began the use of the vaccine after beginning to cough, the more prompt was the response, and in two cases, undoubtedly exposed, and beginning to cough, the disease was abated. At least all cough ceased and there was no further trouble.

"Of course regularity of injections and persistence of treatment are essentials for success. Early in our series we had much trouble from both causes. The past two months particularly, our patients mostly have reported regularly and until discharged. We interpret the present regularity of attendance to the eagerness of the mothers to benefit their children. They are not slow to note improvement, and we almost know after the 3rd, 4th or 5th injection very marked evidences of benefit will be reported.

"While the disappearance of the whoop is used to indicate the end of the paroxysmal stage, be this short or lengthened, the benefits of the vaccine from seven to ten days after beginning (and this means 3 to 5 injections) are in evidence in producing marked subsidence of all symptoms—longer intervals between coughing, lessened severity, less vomiting, and last, but not least, better sleep, and better appetite.

"The needle seemed to act as a deterrent in our early cases, but it is now accepted as a much easier measure than forcing medicine down a child's throat every two or three hours, only to provoke a paroxysm and have it vomited.

"Prophylaxis.—To date we have had the opportunity of giving vaccine to 17 patients, unquestionably exposed to pertussis but not showing symptoms, and of this number not one developed the disease.

"For immunity we have endeavored to give three injections within the week, though one received but two in-

jections and one received the first and third injection twelve days apart.

"The immunity injections were one-half c.c., 1 c.c., and 2 c.c. of the vaccine, though one patient, three weeks old, received one-fourth, one-half and one c.c. of the vaccine respectively, for the three injections. I should not now hesitate to give the full immunity dose for a new-born infant.

"Luttinger and others report almost absolute immunity, the result of the use of the vaccine for protection.

"If the suspicion could in any way be aroused or entertained that the vaccine did not give decidedly positive results as a curative agent, as a prophylactic, there can be no dispute as to its efficiency.

"I am well aware I have left myself open to criticism for not reporting any controls, but after noting the prompt effects of the vaccine upon the disease in the first cases treated, I had not the heart nor disposition to impose a fake remedy for the sake of science.

"The claim also may be made that the present epidemic, from which our patients have been drawn, is a mild one, and that equally good results would have occurred if no treatment or drugs had been used. Inquiry among our mothers does not bear out this claim, for six weeks to two months of the vomiting and whooping have been almost the rule, and many serious complications have arisen. One mother lost two children within three days with pneumonia complicated by meningitis, where no vaccine was used, while a four months' old infant in the same family promply recovered where the vaccine was begun about the tenth day of the disease (case 44).

"I should here state that all the vaccine we have used has been that made by the Bureau of Laboratories, N. Y. Board of Health. It is polyvalent, in that it contains several strains of the pertussis organism and is standardized to one billion organisms to the c.c.

"In the series of cases we have treated, vaccine has been our only therapy, not one particle of medicine or advice of any description, aside from attention to diet and ventilation, has been resorted to; but we firmly believe there are

a number of factors to be added to the use of the vaccine, especially among private patients with means and opportunities at their disposal, where still better results could be attained."

In referring to the tables showing cases treated he says:

"Selecting from Table 2 those cases, coughing 14 days or less, 28 cases we find the average duration of the whooping was 19 1/3 days. Excluding Nos. 8, 12, 25, and 37 for obvious reasons, irregular attendance, and small amounts of vaccine received, gives an average of 16 days for the paroxysmal stage of the remaining 24 cases.

"The remainder of the 52 cases had been coughing and whooping anywhere up to two months, and should not be considered in forming an estimate of the value of any remedy as influencing the paroxysmal stage.

"Observing these cases though from day to day and noting the reports of the attendants, could not but impress one with the value of the vaccine.

"Table No. 3 is appended to show the course of the disease with little or no vaccine, the whoop continuing from 50 to 150 days."

He concludes concerning the use of vaccines as follows:

"Vaccine seems effective in any stage of the disease, and should be given, though the patient is well advanced in the paroxysmal stage.

"As a prophylactic, in our experience, it has been absolute, and every endeavor should be used to induce those who have been exposed, or who have possibilities of exposure about them, to take advantage of the vaccine."

CHAPTER X.

EAR INFECTIONS.

Under ear infections it is well to include infections of the external auditory meatus, because they are usually classed as ear diseases. Of these, furunculosis and eczema are the most important. Furuncles of the auditory canal are particularly painful and often run a prolonged course when immuno-therapy is not employed. The offending organism in the less severe types is usually the staphylococcus albus, while in the more severe types, the staphylococcus aureus is found. These cases yield readily to combined staphylococcus aureus and albus stock vaccines. If treatment is started early, before a necrotic center with pus formation has developed, the infective process can be aborted, with a resulting rapid recovery. Where the infection is farther advanced the immunizing influence of the vaccine will relieve the pain, and the swelling will subside, with a resulting small abscess which can be readily drained and healed. Full sized doses of staphylococcus vaccine should be given by starting treatment with 300,000,000 and increasing the dose to 600,000,000 or more within three or four inoculations. Injections should be made two or three days apart for the first two or three doses, and five to seven days apart thereafter for three or four weeks, so as to build up an immunity and prevent a recurrence.

Eczema of the external auditory canal is usually due to staphylococcus and streptococcus infection. In some cases the colon bacillus is also responsible. Under the various forms of local treatment these cases often prove very obstinate. Good results, however, are obtained from the use of vaccines. A combined streptococcus, staphylococcus stock vaccine gives good results in 30,000,000 to 60,000,000 of the streptococcus and from 200,000,000 to 400,000,000 of staphylococci. Where the colon bacillus is found, doses of

200,000,000 to 400,000,000 of this organism should be given. Inoculations should be made at five to seven-day intervals.

OTITIS MEDIA.

Acute otitis media is practically always due to an extension of the infective process from the naso-pharynx through the Eustachian tube and naturally is due to the same organisms found in infections of the pharynx. The streptococcus and the pneumococcus have a more distinct tendency to infective extension than other organisms found in the nose and throat, and for this reason are most frequently found in acute middle ear infections. The Friedlander bacillus, the micrococcus catarrhalis and the influenza bacillus are also frequently found. After there is an opening through the ear-drum, staphylococci, by migration from the auditory canal, gain entrance to the middle ear and in time the staphylococcus often overgrows and displaces the original infecting organisms so that the staphylococcus may be the only organism found. In cases of chronic suppurating otitis, various organisms like the bacillus pyocyaneus, the colon bacillus, the pseudo-diphtheria bacillus, and the bacillus proteus are frequently found and occasionally we find typhoid or tubercle bacilli.

In the treatment of suppurating otitis with vaccines it is necessary to take this difference in the bacterial flora of the early acute stages and the chronic conditions into account. In the acute conditions early treatment is of great importance, both as a means of relieving pain and to avoid destructive and dangerous extensions of the infection. One of the first symptoms of acute otitis is pain in the ear. When an earache is associated with an acute infection of the naso-pharynx, this is sufficient evidence that the infection has extended to the middle ear and if a vaccine has not been given for the existing "cold," it should be employed at once for the ear complication. If there is bulging of the

drum it should be lanced, but if the infection has not advanced sufficiently to cause much fluid accumulation in the middle ear, the early use of vaccine will in most instances abort the infection in time to avoid the necessity of opening the ear-drum. Because of the fact that streptococci and pneumococci are the principal offenders, a stock vaccine containing at least these two organisms should be employed, but the combined vaccine usually employed in the treatment of colds serves every purpose. The initial dose should be about 20,000,000 streptococci, 25,000,000 pneumococci, 75,000,000 staphylococci, 60,000,000 micrococci catarrhalis. If no material reaction develops at the point of inoculation a somewhat larger dose should be given the next day. By this time the pain in the ear should be practically gone and inoculations at two or three-day intervals with gradually increasing doses, until about three times the size of the initial dose is given, should entirely clear up the trouble within one or two weeks. Where it was necessary to lance the drum or where the drum ruptured, it will be found that the ear dries up rapidly with a corresponding rapid closing of the ear drum. Where drainage through the tympanic membrane is established, cultures for bacterial examinations should be made and if the patient should not be progressing favorably under the stock vaccine, an autogenous vaccine should be prepared.

The advantages of treating acute otitis in infants and children with vaccines deserve special mention. Local treatment in these cases is always surrounded with much difficulty and as a rule the mother or nurse find it difficult to follow out instructions, whereas a few vaccine inoculations will accomplish infinitely more, while the little patient may be allowed to go without treatment between inoculations.

In cases of chronic suppurative otitis media, the staphylococcus aureus and albus are the most frequent pathogenic factors. For this reason a combined staphylococcus aureus

and albus vaccine in doses of 200,000,000 to 400,000,000 of each organism may be given on a clinical diagnosis for several inoculations and if prompt improvement does not take place, cultures for a bacterial examination should be made to determine the infecting organisms and a corresponding stock vaccine given and, where unusual organisms are present, an autogenous vaccine should be prepared.

Dr. Evelyn Wyman Nagle, of Boston (Results of Vaccine Therapy in Chronic Suppurating Ears, Trans, American Laryngol. Rhinol. and Otol. Society, 1910, and Trans. Ninth Internal Otol. Congress, 1912), has done a most valuable work in demonstrating the advantages of vaccine treatment in cases of chronic suppurative otitis. She reports in all 62 cases treated, with but one failure. Three cases were still under treatment. This should be conclusive evidence to the most skeptical that vaccines are a distinct therapeutic aid in the treatment of these cases. She employed autogenous vaccines in all these cases. Her method of procuring cultures consisted in cleansing the aural canal with alcohol and after wiping away the alcohol, the pus was forced out of the middle ear by means of a Eustachian Catheter. This insured a culture from the source of the infection.

From a review of the literature on this subject it is apparent that some cases are not benefited by vaccines even where the utmost care is employed in the selection of a vaccine and its administration. In many of these cases, there is, in all probability, some necrotic bone present in some obscure place, while in others the conditions of the tissue cells in the infected area has become such that a tolerance to the infecting organism has been created to a point where immunizing responses can no longer be aroused. This should emphasize the importance of always employing vaccines in the acute cases, where uniform good results are obtained, and by this means prevent the development of an unfortunate chronic condition.

Dr. George M. Coates (The Laryngoscope, July 1914), for the purpose of determining the therapeutic advantages of stock vaccines in the treatment of suppurative otitis media, treated a number of cases at the Polyclinic and at the Pennsylvania Hospital, Philadelphia, and will quote as follows:

"The conditions under which this trial was carried out were therefore made precisely similar to those of cases treated in the heart of the country districts, and were made as rigid as possible. In other words no other treatment was given, the causative organism was not ascertained by culture and the dosage was made dependent on clinical observation. The Social Service Department was of great use to us in bringing back, for observation and treatment, cases who became negligent about regular attendance, and its workers are most enthusiastic about this method. The cases were taken just as they presented themselves, acute, sub-acute or chronic, and many of them were those who had run the gamut of methods of treatment, other than vaccines, without result. I shall not give the detailed histories at this time as this is merely a preliminary report on this phase of the subject, and a summary of the results obtained is enough for a paper of this description.

"Two formulas were used chiefly, as follows: The first contained Friedlander's bacillus, 300,000,000; micrococcus catarrhalis, 200,000,000; pneumococcus, 80,000,000; streptococcus, 60,000,000; staphylococcus albus, 200,000,000; staphylococcus aureus, 200,000,000, per cubic centimeter. The second formula was: Streptococcus, 100,000,000; pneumococcus, 100,000,000; staphylococcus albus, aureus and citrius, each 200,000,000; and colon bacillus, 200,000,000.

"The technic was simple: The arm was scrubbed with alcohol and the injection given just beneath the skin and above the elbow. This was repeated at 48-hour intervals in the acute cases, and at three or four-day intervals in the chronic ones, alternating from one arm to the other. If results were not obtained after a few injections with one formula the other one was tried, and sometimes the two formulas were used alternately. The only reactions ob-

served were the hyperemias surrounding the site of the injections for the first two or three doses, usually fading out in 24 to 48 hours. Eleven cases showed no hyperemia at all, and in three it was intense and accompanied by considerable induration, which, however, subsided in one or two days without any further treatment than another injection of the same vaccine at the same place on the same arm.

"In the acute cases the best results were obtained by giving slightly larger doses at shorter intervals, namely, 48 hours. The average initial dose for all types was 0.2 c.cm. for children under three years of age, 0.3 to 0.4 c.cm. for those from three to six years, and 0.5 c.cm. for all over that. This dose was doubled at the second and third injections and, when the ear became dry, two injections of the maximum dose were given at three-day intervals to ensure permanency. In small under-developed children the dose was made smaller than that I have mentioned, and the maximum dose for adults was about 1.5 c.cm. In the favorable cases an increase of discharge was noted after the first and sometimes after the second injection, but the discharge became more serus in character. In the majority of cases the external canal was only damp after the third or fourth injection and dry at the fifth.

"Sixty-three cases were treated altogether and of these 56 were apparently cured, although several of them became dry, relapsed, usually through non-attendance, and then, on resumption of the treatment, again became dry. Two cases were improved only, and five were unsatisfactory. These five cases were all of a severe type with fetid discharge and granulations. These were cultured out to determine the cause of the failure and gave the following results:

"One showed diphtheroid bacillus and pneumococcus, one tubercle bacilli and pneumococcus, and two pneumococcus and bacillus pyocyaneus. They are now under treatment with autogenous vaccines.

"While none of these cases have been dry for a long enough period of time—six months being the maximum—to say that they are permanently cured, yet the results obtained are sufficiently striking to warrant further trial of this easy method, particularly as no bad results have been

observed. It has also been used in a number of acute cases in private practice with uniformly good results although these are not included in the above series. In the series of dispensary cases, seventeen were acute or sub-acute (several with mastoid tenderness) and 46 were chronics extending over periods varying from six months to many years' duration."

In a later paper (New York Medical Journal, July 10, 1915) Coates says:

"For acute cases which fail to respond to ordinary measures and tend toward the subacute and chronic groups, the use of vaccines will usually straighten the case out in short order. Once in the group of chronic catarrhal deaf cases, astonishing results cannot be looked for because of the long duration of the process, the changes in the tissues, adhesions, etc. In discussing the curative value of vaccine treatment in aural conditions, we must not forget that many acute cases will improve with little or no treatment, also a large majority of the remainder, if carefully looked after in the usual manner. Therefore, to determine the value of any form of treatment, it is necessary to show in a large series of cases, that the time of convalescence has been materially shortened. This was shown conclusively by Weston and Kolmer at our Philadelphia Hospital for Contagious Diseases in 1910-11, when, by autogenous vaccines in cases of scarlatinal otitis media suppurativa, they were able to increase the proportion of dry ears obtained in 30 days or less from 7 per cent to over 22 per cent. I am quite convinced that this method materially shortens the duration of the disease and, if used generally, the average number of days' duration would be much lower.

"The first case in which I ever used vaccines was an acute middle ear suppuration in a child of five years, with considerable fever and mastoid tenderness which persisted in spite of repeated free incisions of the membrana tympani. After three weeks a mastoid operation seemed imminent, but was refused, whereupon I administered an autogenous vaccine, and after the second dose my case was promptly cured, and stayed cured. I have had many such cases."

Dr. Virginus Dabney (New York Medical Journal, Feb. 10, 1912, p. 273) from the reports of other authors and his own work shows that the use of vaccines was instrumental in curing three times as many cases of otitis media in the space of thirty days as was experienced without their use in the same class of cases.

MASTOIDITIS.

The great danger from an acute otitis is extension of the infection to the mastoid cells. When immuno-therapy is applied sufficiently early this complication can be avoided. If the infection has already extended to the mastoid a dose of combined streptococcus-pneumococcus-staphylococcus vaccine should be given at once. In such cases the infection is usually so extensive that about two or three times the size of the initial dose employed in an acute otitis should be given, and the same dose repeated at one to three-day intervals. Cultures should also be made for bacterial examination, and to provide for the possible necessity of preparing an autogenous vaccine.

Dr. S. Moskowitz (New York Medical Journal, August 14, 1915), in a paper entitled "The Newer Therapeutics in Otology," points out that ear cases to a large extent terminate by being operated on or being pronounced incurable. The operations are many times successful, sometimes unsuccessful, with many fatalities. The paper is devoted to purulent otitis media and mastoiditis. He began to use vaccines in virulent otitis in 1910, with very satisfactory results, usually employing combined stock vaccines containing the usual infecting organisms present in these cases. The results were not only good in cases of purulent otitis, acute and chronic, but he was also surprised to find good results in a number of mastoid cases where the course of the infection was aborted. In referring to Dr. Haskins' work he says:

"All through Dr. Haskins' paper one finds such reports as the following:

" 'Case No. 3 of Table 2: Had four operations, last four years ago. Discharge persistent. Vaccine used, ear dry after tenth injection. Cured. Case No. 7: Mastoiditis treated for nine weeks. Refused operation. Received four doses autogenous vaccines, ear dry after second dose and remained so. Cured. Case No. 13: Operation advised Aug. 15, 1913. Discharge persistent until Jan. 2, 1914. Ears became dry after five doses.'

"In my own cases I will show these statements to be absolutely accurate. In the above mentioned papers we have the clinical and laboratory theories put into actual use, and they are correct. It is to be noted that in chronic suppurative cases no influenza or pneumococcus micro-organisms were found, showing that they do not persist long after acute suppuration becomes chronic. This fact I have also observed."

His case reports are very instructive and I will give them as follows:

"Case I. E. C., boy, aged 10 years, of previous good health, except for recurrent attacks of tonsillitis. Developed sudden acute pain in both ears, worse in the right. With the pain there was high temperature, shooting up and down. For a few days previous to this attack, complained of a slight cold from careless exposure. Examination of ears revealed both drums bulging, which were promptly incised, and got pus in quantities from both ears. The discharge continued for two days, and so did the high temperature to about 100 degrees F. The left ear was almost well on the third day and the right ear was still painful and discharging.

"Examination revealed in the right ear discharge coming with pulsation, and with otoscopic suction there was brought into view much more pus. Right mastoid very tender, especially around the tip. Left ear, no symptoms. Diagnosis: Mastoiditis.

"Used vaccine containing pneumococcus, influenza bacillus, streptococcus, and staphylococcus albus, aureus and citreus. After second injection there was no tenderness to

speak of, and after the fourth no discharge. Discharged, cured, on the tenth day of the disease. Patient had no further trouble, except that later on I enucleated the tonsils and removed the adenoids present, as a prophylactic measure.

"Case II. In January, 1912, was called to see a woman suffering from a purulent discharge from the right ear and very tender painful mastoid on the same side. Temperature 101 degrees F. Patient looked extremely anemic and septic. She had an acute double otitis from coryza and heavy cold. Within the last two days her physician and a consulting otologist diagnosed her condition as mastoiditis, and on the same day as my visit an eminent otologist also diagnosed it as mastoiditis, and strongly advised an immediate operation. On account of the severity of the case, the tenderness of the mastoid, and the septic look of the patient, I was most inclined to advise operation. This she absolutely refused, and for this reason I suggested the use of the vaccines for a 24-hour trial as the only alternative.

"A first injection of stock vaccine was given immediately, the second being given on the evening of the second day, with marked improvement on the morning of the third day. The discharge was stopped and the pain now became very much less and the tenderness of the mastoid was also very much better. After five injections the patient was cured, except for a certain amount of defective hearing. This was treated with the usual methods and after a couple of months the patient was in excellent condition.

"Case III. Miss M., aged 19 years, consulted me a second time for a discharging ear which she had since childhood. At her first call to my office she asked for relief from vertigo, discharge, tinnitus, mastoid pain, and right-sided cephalalgia. This was two years ago. At that time she was given bichloride douches one in 4,000, and argyrol drops, which were followed by boric acid in alcohol drops, at home. At the office she was given otoscopic suction (passive hyperemia and mechanical removal of discharge). She improved rapidly and after two weeks' treatment stopped coming, owing to the fact that she lived at a great distance and that she thought she felt 'all well.' The otoscopic picture at that time was a small perforation of the drum with hammer

handle exposed and foul discharge. She returned to my office, Sept. 22, 1914, with very severe symptoms; an acute exacerbation, with violent pains in the ear, over mastoid and right side of head. She also complained of vertigo, which was almost constant and worse on the slightest bodily exertion. There was an up-and-down temperature daily. Discharge was very profuse and foul-smelling.

"On examination of the ear I found almost the whole drum membrane gone, much granulation tissue, and the discharge pulsating synchronously with the heart-beat. Mastoid tender over cells and tip. The day previous to her coming to my office the patient had been to the Manhattan Eye and Ear Infirmary, where two prominent surgeons whose names were mentioned to me had advised her to be operated on at once, for mastoiditis. She refused operation, despite the fact that she was told that her case was a very serious one.

"At my office her ear was cleansed and a culture taken for autogenous vaccine, and she received that day an injection of stock vaccine, containing 30,000,000 each of staphylococci, streptococci and influenza bacilli respectively. The streptococcus was used as the severity and high temperature and also the glandular enlargement suggested. The staphylococcus was used as it is usually a complicating factor in chronic relapses. The influenza bacilli were added on account of a prevalent epidemic at the time and her own clinical history. Report of culture came back 'almost pure culture of streptococci.'

"In 24 hours there was a suggestion of improvement after the first stock vaccine injection, and on the third day the patient was decidedly improved, and being that the patient responded so well to this vaccine it was continued every second day. On Oct. 1, 1914, the ear was dry, and all the symptoms she had were slight occasional pains and attacks of vertigo; the fact was noted by the patient that her hearing was much better than it had been. From that time on injections were given about bi-weekly until all symptoms subsided and she was discharged a month later feeling very well and making no complaint. Heard of patient during the present writing, to the effect that she was well.

"This shows the remarkable effect of the stock vaccine of a good manufacture, which I believe the one I used to be, from repeated experiences in a great many instances. Furthermore, I have never seen any ill effects whatever from its use.

"Case IV. Mrs. G., aged 50 odd years. Personal history: Had always been ailing more or less for a great many years. Several days before the onset of her present trouble was in contact with a relative suffering from pneumonia. On Dec. 30, 1914, was taken ill with a sudden severe cold and pain in the left ear, and a physician, said to be an otologist, was called in and made light of the case. Drops were prescribed and after he left the patient kept getting worse and had a very bad night. Pains spread to the back of the ear and top of the head. Patient also complained of very annoying tinnitus and throbbing in the ear. On the morning of the following day I was called and found the patient suffering intensely and severely prostrated. Drum had spontaneously ruptured, giving but slight relief. I immediately enlarged opening by making a free incision.

"On account of the history, diagnosis was made of acute otitis media purulenta, with beginning mastoiditis, and on the evening of my first visit it was a marked case of mastoiditis, with very severe symptoms and cerebral involvement. Patient had very severe pains in ear and over mastoid, also very bad pains in the head on the same side, and slight stiffness of the muscles of the neck. After the incision the ear began to discharge freely, but there was not much relief in the symptoms.

"An injection of vaccine was given containing pneumococcus, streptococcus, and staphylococcus, and this was continued daily, during which time the discharge continued for a week without lessening, although the symptoms subsided. At the end of the second week patient was very much better, temperature was normal and remained so, and all that the patient complained of was the tinnitus and small amount of discharge. At the end of the fourth week the patient was discharged, feeling very well, the hearing fair and improving.

"The usual treatment was given in this case, such as the

bichloride douches, antiseptic drops, argyrol for the first few days, later the boric acid in alcohol. The ice bag was also used a great deal of the time and seemed to give very much relief."

McKernon (Trans. American. Laryngol., Rhinol. and Otol. Society, 1910) points out that cases of mastoiditis operated on after scarlet fever have a tendency to heal slowly and that to some degree this held good with measles, but with the use of vaccines these cases healed rapidly and the discharge from the ear was of short duration. He employed autogenous vaccines.

The importance of therapeutic immunization in acute middle-ear infections is not sufficiently appreciated. These ear infections are too serious to allow them to progress without employing all the means at our command to stop the progress of the infection. One of the saddest cases in my experience was a mastoid that developed from an acute otitis. This was the only daughter of a widow. Her mother had worked hard to send her through school to become a teacher. While she was still going to school I treated her for an acute otitis by lancing the eardrum and antiseptic flushings. About six months after she began teaching in a public school she had another attack of acute otitis media; I again lanced the drum and used antiseptic washes. She did not improve and was placed in a hospital by the teachers' association, in charge of a specialist. She was operated on and three weeks later died from infective extensions to the brain. Vaccines were not in use at that time, but from what experience I have had there is no doubt in my mind but that her life could have been saved if vaccines had been available. I am sorry to say that many physicians allow their acute ear cases to progress, even at this late day, without availing themselves of the advantages of therapeutic immunization, often resulting in chronic suppurating infections with impaired hearing and not infre-

quently in death. The time to avert danger is to institute the best treatment before the danger point has arrived. The early use of a mixed stock vaccine containing the organisms that cause dangerous mastoid infections is the safest and surest method of avoiding the development of a mastoiditis.

VERTIGO.

Continued experience with the use of the bacterins in the treatment of vertigo and extensive investigation into the etiology of this disease confirm my early inference that this disease is caused by an inflammatory process due to chronic infection of the internal ear apparatus, more particularly the semicircular canals or the nerves leading to them. That the cause of this disagreeable ailment has been traced to disturbances in the internal ear is indicated in an exhaustive article by Dr. George E. Davis, who concludes:

"The internal ears are the special sense organs of equilibrium. With the internal ears we recognize (orientation) and maintain our relations to space (equilibration).

"The visual sense organs (the eyes), and the kinesthetic sense organs (the muscles, etc.), are accessory sense organs of equilibrium (the internal ears), through the mediation of the cerebellum.

"The two special sense organs of equilibrium (the internal ear on either side), are normally symmetrical in structure and function, and any factor whatever, whether it be physiologic, experimental or pathologic, which enervates, stimulates or irritates one of these twin organs in excess of the other (or on the other hand accomplishes the same thing through enervation, depression or destruction of one in excess of the other), in that measure tends to or creates proportionately a disturbance of equilibration sufficiently marked or intense that we also get nystagmus and that unpleasant and complex phenomenon termed vertigo."

Dr. Edward Bradford Dench (New York Medical Journal, Jan. 6, 1912, p. 1) reports a number of cases of vertigo

treated by operation and other methods, and among other things says:

"As the end organ of the complex mechanism controlling the equilibrium of the body is situated in the semicircular canals, all cases of vertigo must, in their broadest sense, be considered as aural vertigo, inasmuch as they represent an involvement either of the ear itself or of some portion of the auditory nerve trunk or of its central or cortical filaments.

"We may classify cases of this disease as follows:

"1. Cases due to a chronic non-suppurative inflammation of the middle ear.

"2. Cases due to a residual suppuration of the middle ear.

"3. Cases due to aural suppuration.

"4. Cases due to involvement of the auditory nerve trunk, as the result either of a specific inflammation involving the nerve trunk, or due to a degeneration of the end-organ of the auditory nerve as the result of some middle ear inflammation or of some general diathetic condition.

"It should be borne in mind that when any portion of the auditory apparatus, either of the middle ear, the labyrinth, or the nerve trunk, is in a pathological condition, any slight stimulus, particularly an increase in the blood pressure, may be sufficient to bring on an attack of vertigo."

I will briefly review his cases because they are specially instructive in showing the relation of inflammatory processes of the aural mechanism to the production of vertigo.

Case 1. Non-suppurative otitis media with tinnitus was successfully treated with a two-per-cent solution of pilocarpin introduced into the tympanic cavity through an Eustachian catheter.

Case 2. Another case of chronic non-suppurative otitis media with progressive sclerotic changes within the middle ear and labyrinth was treated by opening the vestibule with

a small knife and allowing a certain amount of the labyrinthine fluid to escape. This aggravated the vertigo for a time but the condition gradually subsided and finally recovered.

Case 3. One case of grippe was followed by acute otitis media with mastoid involvement which was operated upon six weeks after the initial attack. A month after the mastoid operation severe vertigo suddenly developed. The acute symptom subsided but a slight vertigo remained, and two months later a radical operation was performed relieving a fistula in the horizontal semicircular canal. Drainage was instituted and the patient made a complete recovery.

Case 4. This was a case of perilabyrinthinitis with ver- and was almost entirely deaf. As no fistulous opening into the labyrinth was found, the radical operation was performed and primary grafting employed. The patient made a good recovery.

Case 5. This case gave a syphilitic history. The patient complained of hardness of hearing with vertigo. He was given large doses of salicylate of mercury and began to improve at once under this treatment and completely recovered. In some special remarks on this case the author says: "In this case we had to deal undoubtedly with a syphilitic inflammation, either of the auditory nerve trunk itself or of the meninges in the immediate neighborhood of the internal auditory meatus." The complete recovery of the patient confirms the correctness of the diagnosis.

Case 6. This man showed involvement of the auditory nerve trunk with severe tinnitus and some vertigo. Operation of dividing the auditory nerve at its emergence from the base of the brain was performed, and the patient was absolutely relieved for a number of months. There was some slight return of the tinnitus, but the other conditions remained good.

These cases show that a large variety of inflammatory conditions in and around the internal ear may be responsible for the single symptom of vertigo. In cases 3 and 4 operations were performed for the purpose of establishing drainage, but unfortunately no report of bacterial findings was made to show the etiological cause of the inflammatory condition.

The syphilitic case demonstrates that a specific causative organism—the spirochete—may be responsible for an inflammatory process that will subside under specific treatment, with a resultant disappearance of the vertigo.

Putnam (Therapeutic Gazette, Feb. 15, 1912, p. 119, review Boston Medical and Surgical Journal, Sept. 28, 1911) says:

"The functional efficiency of the apparatus of which these canals are an essential part may be impaired, even though the cochlea and auditory apparatus are in a normal state, so that tests for hearing are an insufficient guide in the determination of the labyrinthine condition in cases of aural vertigo."

It is now quite generally admitted that aural vertigo is associated with some inflammatory condition connected with the semicircular canal and that this inflammation may be acute, subacute or chronic. It is also found that when such inflammation exists, variations in blood pressure have a great influence on the vertiginous attacks, causing them more frequently when the blood pressure is high than when it is low. This would indicate that in cases of arteriosclerosis the attacks of vertigo are due primarily to an inflammatory condition of the aural apparatus while ordinarily they are attributed to the sclerotic condition.

Cases of vertigo associated with suppurative and non-suppurative otitis media are commonly met with. Bacterial examinations of this pus in the early stages of this disease show that in a large majority of these cases the

streptococcus is the primary infecting organism. After a rupture of the ear drum, outside contamination soon takes place and staphylococci are found. Later they often supplant the streptococcus. From clinical observations we find that the streptococcus is an organism that may cause an almost endless variety of inflammation and many kinds of tissue may be involved.

I have seen cases of chronic erysipelas where the inflammatory process was practically the same for months. Chronic rheumatic joints are good illustrations of persistent infective processes without pus formation. As streptococcus infections are of such common occurence in middle ear inflammation, the inflammatory processes associated with vertigo can very readily be attributed to this organism.

In chronic nonsuppurative otitis we have a subdued inflammation associated with inflammatory deposits and adhesions. This condition often extends into the bony structure around the semi-circular canals without pus formation. This is quite similar to the condition in the bony structure of enlarged joints in chronic rheumatism. From our present knowledge of germs and their relation to inflammatory processes, the inference is conclusive that the inflammatory process in these cases of vertigo is due to an infecting organism. It seems entirely probable that the streptococcus is responsible for many of the conditions which produce vertigo. Streptococcus vaccine is the specific for streptococcus infections and my experience which now includes the successful treatment of twenty-four cases of aural vertigo with this vaccine, seems to conclusively show that this inference is well sustained.

A somewhat detailed report of several of these cases will be of particular interest as the subject is barely mentioned in present day medical literature.

Case 1. A man called at my office for treatment. He

was tall, well developed, and appeared in good health, but complained of persistent attacks of vertigo. This condition was steadily growing worse, although he had been under the care of one of the best physicians in Detroit for four months. He was a foreman in a pattern shop, and found it difficult to walk about to attend to his work. No well-defined reason for the vertigo could be found. There was no tinnitus and hearing was normal. The ear drums were also normal. On careful investigation I realized that by giving medicines probably nothing more would be accomplished than by the previous treatments. Shortly prior to that time I had treated a case of nasal catarrh with streptococcus vaccine in which a peculiar dizziness or "nervous dancing of objects," as the patient described it, was incidentally completely relieved. From this clue I decided to treat the case empirically with streptoccus vaccine, giving 30,000,000 with each inoculation at seven-day intervals. After the second dose he was much improved. Treatment was continued for two months, and a complete cure was effected. It is now nearly eight years since treatment was started and the vertigo has not returned.

Case 2. A man working in the dynamo room of a large power plant would be seized with spells of vertigo sufficiently severe to cause him to fall to the floor. He had been treated by several physicians, but was steadily growing worse. His hearing was good, but he complained of tinnitus in one ear. Four doses of streptococcus vaccine at intervals of one week effected a cure. A year later the vertigo returned. This time it required six doses to effect a cure. About fourteen months after the second attack the vertigo returned again, when but two doses of streptococcus vaccine were required. There has been no return of the vertigo.

Case 3. I was called to treat an old lady having vertigo

with a vaso-motor disturbance which caused the skin to become markedly flushed. The vertigo was persistent whether walking or lying down, and was so severe that she could not walk across the room unaided. This condition existed for some months. I persuaded her to allow me to treat her with vaccines. When I called to give her the third dose she sat in the hall at the open door. Expressing my surprise at seeing her there, I asked how she got downstairs. She informed me that she walked down alone and in my presence she walked upstairs to her room alone. The improvement in her vertigo was remarkable. She very much disliked hypodermic injections, but I managed to get her to take the third dose. I have since lost track of her and am unable to say how she is now.

Case 4. A young woman with previous good health had been under treatment by a physician for seven months for vertigo and other disturbances that went with it. She had some neuralgic pain on the left side below the heart. The appetite was poor and she had lost 20 pounds in weight, weighing at the first visit to my office 108 pounds. She described the sensation as being similar to that of riding in a small boat on rough, rolling water. The vertigo improved steadily after using the streptococcus vaccine and after taking ten doses she was entirely restored to health.

Case 5. A middle-aged man employed as a wagonmaker complained of vertigo of six weeks' standing with tinnitus in the right ear. The vertigo entirely subsided after the sixth inoculation of vaccine.

Case 6. A middle-aged lady complained of tinnitus in the ear with vertigo and difficulty of hearing. This condition had existed for about three weeks. After three inoculations her vertigo disappeared and the hearing was materially improved.

Case 7. A man employed as chief electrician in a large

power plant consulted me concerning a vertigo of five months' standing. He described his condition as "feeling about half drunk all the time." There was no apparent ailment that the condition could be ascribed to. Hearing was normal and the habits were good and regular. I gave him inoculations of streptococcus vaccine at seven-day intervals. He began to improve after the first inoculation and was completely cured after five doses. It is now seven years since the last treatment with no return of the vertigo.

Case 8. A middle-aged man who had charge of the power plant in a large manufacturing establishment, after a bad cold, had some pain in his ears with a fullness in the head. Hearing was somewhat impaired and vertigo was almost constant. This had been going on for four weeks. Streptococcus vaccine was employed and four doses were given from five to seven days apart. Improvement was observed after the first inoculation and the man made a complete recovery. As one of the members of the family was sick with tuberculosis. I had occasion to see the man frequently and he assured me that there was not the slightest return of the vertigo.

Case 9. An elderly lady complained of being almost deaf for about one week. She also was troubled with several attacks of vertigo. Examination showed that the hearing was almost entirely gone in the right ear and she could only hear loud conversation with the left. There was no pain or apparent inflammation in either ear. Streptococcus vaccine was given for the first dose and a streptococcus-staphylococcus combined vaccine was given a week later. Two weeks after the first inoculation, when the third dose of the combined vaccine was given, the vertigo had left her but her hearing was not improved. I have lost track of her and do not know what the ultimate result was.

Case 10. A young woman of 29 had suffered with repeated attacks of vertigo for four months. Hearing was

normal. There was some digestive disturbance and the question as to whether or not the vertigo was due to nausea was carefully considered. I found that it was not. In consideration of the digestive disturbances I gave her a combined colon bacillus and streptococcus vaccine. Six doses at weekly intervals effected an entire cure.

Case 11. This was a man 74 years old with marked arterial sclerosis. Attacks of vertigo would come on at intervals several times a day with great severity. During these attacks he was obliged to sit down or take hold of some object to keep from falling. His hearing was somewhat impaired but he could hear a loud conversation quite well. His general health was run down and he had in a degree lost control of co-ordinating the legs while walking. Streptococcus-staphylococcus combined vaccine was given at from five to seven-day intervals. He had a single attack of vertigo after the first inoculation. I gave him altogether ten doses with the idea of procuring the tonic effect of the vaccine. His general health improved some, but the treatment was discontinued. So far as I know the vertigo has not returned.

Case 12. An apparently well-preserved old lady complained of severe tinnitus, taking on the form of music and imaginary people talking to her. This annoyed her so that she could not secure proper sleep. Her hearing was fairly good. The vertigo was quite severe. I gave her seven doses of combined streptococcus-staphylococcus vaccine. Her vertigo soon left her after using the vaccine and the tinnitus became some better but was still troubling her when I lost track of her.

Case 13. Man with vertigo of two years' standing. Tinnitus in both ears. Hearing normal. Three doses of streptococcus at weekly intervals relieved him of his vertigo but the tinnitus was not materially improved.

Case 14. A case of chronic non-suppurative otitis with

tinnitus in both ears. Can only hear loud conversation and has been suffering with a vertigo which came on gradually for some time. The patient also had some bronchial trouble at the same time. I administered seven doses of streptococcus-staphylococcus-pneumococcus combined vaccine at about weekly intervals. The vertigo subsided soon after using the vaccine and tinnitus and hearing improved. Two months after receiving the last dose she returned, complaining of some dizziness. I started the vaccine treatment again and the vertigo subsided after the first inoculation, and after a few more inoculations recovered.

Case 15. Chronic non-supperative otitis in a man of 60 with vertigo of seven years' standing. At first the vertigo was intermittent, but for the past year it has been almost constant. He reports that some days the vertigo was so bad that he was obliged to sit in a chair all day. The hearing is such that conversation can be carried on with a moderately loud voice. The vertigo began to improve after the first inoculation of streptococcus vaccine and after the third dose it had entirely left him. Treatment was continued for some time with the hope of improving the hearing, but that was finally abandoned.

Case 16. Chronic non-suppurative otitis media with tinnitus and vertigo of four years' standing. During the week prior to the time he first consulted me the vertigo was especially bad. Some days he was obliged to stay at home. The hearing is fair, he can hear a watch tick two inches from the right ear and five inches from the left ear. I started treatment with streptococcus vaccine. Improvement was observed after the first dose and after the third inoculation there was no more vertigo. On account of a concomitant nasal catarrh a combined streptococcus-pneumococcus-staphylococcus vaccine was employed for some time, resulting in a complete cure.

Case 17. A case of chronic non-suppurative otitis media

in a woman with vertigo of over a year's standing and tinnitus in both ears. Cannot hear a watch tick next to the ear. Bone conduction poor. Recovery from the vertigo after eight combined streptococcus-staphylococcus vaccine inoculations.

Eight other cases of vertigo were successfully treated, the details of which would not materially add to what has been said in my other cases.

Dr. Harold Payne Lawrence, of Pinconning, Mich., courteously reports the following case: "Mr. D., age 48, musician, consulted me in regard to case of vertigo to which he had been subject for one and a half years. A number of internists had diagnosed his trouble as autointoxication, but the treatment was of no avail. I also diagnosed his trouble likewise, but failed to benefit him. He then told me he suffered from a running ear several years ago and that naturally drew my attention to the chronic affections of the middle ear. I then thought of a possible infection of the semicircular canals (for which I wish to give thanks to Dr. Emil Amberg, of Detroit, who gave me several valuable hints on the subject). He was injected with the streptococcus vaccine, 60,000,000 every seven days for five weeks, and showed improvement. I was not thoroughly satisfied that the staphylococcus was not also present, so I used combined streptococcus and staphylococcus for six weeks. His trouble has entirely subsided, but he is still under treatment."

The successful treatment of vertigo with vaccine is one more illustration of the very wide scope and real therapeutic advantage of vaccine therapy. In these cases the inflammation is deep-seated in such a position that local antiseptic treatment is practically impossible and operative interference is always a serious procedure. By this simple process of immunizing the patient the trouble may be reached in any part of the body and permanent results procured.

CHAPTER XI.

EYE INFECTIONS.

General Consideration.

In considering the treatment of eye infections with vaccines, the question naturally arises whether immunizing substances which are developed in other parts of the body can be conveyed by means of the blood to the non-vascular structures of the eye, like the cornea lens, vitreous, etc. To answer this question, Morax and Soiseau (Annales de l'Institut Pasteur, Nov. 9, 1911) made some investigations with animals immunized to diphtheria and tetanus. They found that the aqueous in healthy, highly immunized animals contained proportionately less antitoxin than the blood serum of the same animal; but on retapping they found the antitoxin content of the aqueous very much increased. This shows that the increased blood supply incidental to the traumatism caused by withdrawing the fluid from the anterior chamber of the eye enlarged the channels enough to allow a free access of the antibody in the blood to the non-vascular structure of the eye. Irritation due to an infection will similarly increase the channels to allow a freer supply of the immunizing substances contained in the blood to the non-vascular structures of the eye.

From this it would seem difficult to overestimate the importance of applying immuno-therapy in infections which involve the non-vascular structures of the eye. It is well known that when infecting organisms gain lodgment in the tissues where immunizing substances are not readily available, the infections are liable to become destructive in character. This applies with unusual significance to the eye, in view of the importance of the organ and the amount of serious permanent damage that may follow even a small amount of tissue destruction. It does not require much of a central corneal ulcer to permanently impair vision. Let

us take, for example, a corneal ulcer due to a streptococcus or pneumococcus, in a case where the immunizing resistance to these organisms is comparatively low. A corneal ulcer is necessarily too small a lesion to arouse systemic reaction enough for so much production of antibodies that an adequate amount of them will find their way to the site and destroy the infecting organism before irreparable damage is done. But by injecting a bacterial vaccine under the skin a very large amount of tissue, as compared with that involved in the corneal infection, is actively called into service for antibody production. This antibody is then conveyed, by means of the circulatory system to the infected cornea and aids in destroying the germs long before it would have been possible for the infection in the cornea to stimulate an equal amount of antibody production.

What is true of corneal infections applies equally to infections of other non-vascular structures of the eye. Eye infections are quite common and are met by the general practitioner almost as frequently as by the eye specialist. Early immunization being of so much importance, it is necessary that the general practitioner should familiarize himself with the bacteriology and vaccine treatment of eye infections, because he is often called to treat these cases before an eye specialist is called into service.

HORDEOLUM.

Styes are not properly classed as eye diseases, because they are nothing more than small furuncles in the margin of the eyelids. The staphylococcus albus is the organism most frequently found. In the more severe cases the staphylococcus aureus is usually found.

A combined staphylococcus aureus and albus vaccine given in 200,000,000 to 500,000,000 doses at three to five-day intervals serves every purpose with but few exceptions. Improvement may be looked for in a few days, and if treat-

ment is continued for several weeks permanent results will be obtained. In specially obstinate cases treatment should be continued for several months to prevent relapses.

CONJUNCTIVITIS.

Conjunctivitis is seen in acute and chronic forms. The important varieties are caused by the gonococcus, pneumococcus or streptococcus. The staphylococcus is also found; but usually as a secondary invader after the other organisms have paved the way.

Where a purulent conjunctivitis exists in patients having gonorrhea it should be regarded as gonorrheal until otherwise determined by bacterial examination. Gonorrheal conjunctivitis is always a serious affair. Often the intense inflammatory condition causes so much swelling that the pressure from the swollen tissues interferes with the nutrition of the cornea, resulting in corneal ulceration and not infrequently total or partial destruction of the cornea.

Here the early use of gonococcus vaccine is of utmost importance. By immunizing against the infection, deep-seated tissues will not become involved and where extensive swelling exists it will subside. It appears that in such cases the best results are obtained by giving large doses.

From the literature on this subject it seems that indifferent results were obtained by giving small doses ranging from two to ten millions. Allen recommends 250,000,000 of stock vaccine to be given at once after making a diagnosis. He reports four cases in which marked beneficial results were obtained by this method. I have given 50,000,000 stock gonococcus with good results in one case, making inoculations at five-day intervals. In gonorrheal conjunctivitis appropriate local treatment should not be neglected while using the vaccine.

SIMPLE CONJUNCTIVITIS.

Streptococcus conjunctivitis is met with in every form, from an extremely acute inflammation with much swelling to a comparatively mild condition. In cases of pneumococcus conjunctivitis there is usually not so much swelling. In many cases we have mixed infections of both organisms and the staphylococcus frequently also becomes an additional invader. The early control of these cases is essential because of the danger of corneal involvement, especially where much swelling causes pressure and resulting interference with corneal nutrition.

As a rule, the general practitioner is not in a position to make a bacterial examination at once in these cases, and early vaccine treatment being important it is entirely sound to give a combined stock vaccine consisting of streptococci, pneumococci and staphylococci. My experience with this method has been so satisfactory that I would consider it gross negligence not to give these cases the benefit of the vaccines. Treatment should be started with the average dose and in bad cases it is advisable to repeat the inoculation in 24 hours. In less severe cases injections should be made from two to four days apart.

Cases of severe conjunctivitis are often met with in infants a few weeks old, where the infection is due to a staphylococcus. They are often very persistent and not infrequently resemble gonorrheal infection. Staphylococcus vaccine given in 50,000,000 doses repeated at three or four-day intervals is of great value in these cases. Conjunctivitis may also be caused by colon bacilli, bacillus pyocyaneus and other organisms when corresponding vaccines should be employed in the usual dosage.

CHRONIC CONJUNCTIVITIS.

Chronic conjunctivitis is sometimes due to the Friedlander bacillus, but more frequently to the bacillus lacuna-

tus. A careful diagnosis from bacterial examination is always necessary in these cases. Being of a chronic nature a few days delay in treatment while the examination is made does no particular harm. Cases caused by the Friedlander bacillus respond poorly to local treatment but are amenable to the Friedlander bacillus vaccine. Treatment should be started with 200,000,000 and repeated at four or five-day intervals with gradually increasing doses. Good results are obtained with the vaccine treatment in chronic conjunctivitis caused by the bacillus lacunatus of Morax-Axenfeld. He advises starting treatment with 100,000,000 organisms and repeating inoculations at from seven to ten-day intervals. If prompt relief is not obtained after two or three inoculations the dose should be increased to 250,000,000, when good results are usually obtained.

DACRYOCYSTITIS.

Dacryocystitis is nearly always caused by the streptococcus and frequently follows acute conjunctivitis. Where an abscess has formed and opened through the skin, staphylococci are also found. Combined streptococcus and staphylococcus vaccine has given me none the less brilliant results in these cases. If the vaccine is given early, the inflammation will subside without pus formation, and where pus must be evacuated the inflammation subsides promptly with a rapid healing of the wound. An important factor of the vaccine treatment in these cases is that from the short duration of the inflammatory process fistulas and obstructions of the lachrymal canal are avoided if vaccines are employed reasonably early.

KERATITIS

Corneal ulcers seem to be caused by a variety of organisms, the most important being pneumococci, streptococci and staphylococci. I have found these organisms in pure culture and also in mixed infections. They may take an

acute or chronic form, the pneumococcus predominating in the chronic varieties. The micrococcus catarrhalis and the bacillus pyocyaneus are also occasionally found.

As a routine treatment in these cases a combined strepto-pneumo-staphylococcus vaccine gives good results. If prompt relief is not obtained after one or two inoculations bacterial examinations should be made to determine if any other organism is present. In corneal ulcers due to want of a direct blood supply the problem of disposing of the infecting organism is surmounted with difficulties. Ordinarily not much repair takes place until small blood-vessels develop in the cornea to supply nourishment to the ulcerated area. This is always a slow process. With the use of vaccine I have seen these ulcers heal over before the development of an additional blood supply takes place, showing that the blood serum under the influence of the vaccines has developed additional germ-destroying power. A corneal ulcer is such a small affair that practically no systemic immunizing impression is produced, but with vaccines this necessary influence is speedily brought about.

RHEUMATIC IRITIS.

In so-called "rheumatic iritis" we have a disease condition that is not only very painful and distressing but, under conventional treatment, very hard to manage. What is true of the iris applies equally to inflammation of the ciliary bodies. That the streptococcus is the infecting organism in these cases is apparent from the excellent results obtained with streptococcus vaccine.

The following is a good illustrative case: Mrs. R., aged 28, had been sick with acute articular rheumatism for about three months, four weeks of this time having been spent at a sanitarium receiving a course of baths. The rheumatic condition had improved, there being only a slight pain left in the knees. When I first saw her she had been suffering

with iritis for about one week. The attending physician had been using atropine and considering the intensely inflamed condition the pupil was fairly well dilated but irregular. The conjunctiva was deep red and much swollen, so much so that it was difficult to close the eye. The swelling also extended to the orbit, causing the side of the face to be swollen. The pain was very severe at night. The atropine was continued and in addition I gave the patient one dose of 30,000,000 streptococcus vaccine.

The patient told me that in eight hours after the inoculation she began to get relief from the pain and continued to improve. Five days later when I gave her the second dose the swelling and pain were gone, but some redness over the sclera remained. The atropine was discontinued and the inoculations of streptococcus vaccine were kept up at weekly intervals, four doses being given in all. She made a complete recovery.

I have used streptococcus vaccine as a routine in all cases of iritis where there is no history of syphilis with uniform good results. The relief from pain in these cases is so marked that the value of the vaccine at once becomes apparent to the patient.

Sympathetic Ophthalmia.

In sympathetic ophthalmia we have an inflammatory process that is not easily accounted for, but from what is known about infecting organisms it is quite probable that these cases are caused by the usual pus cocci extending from the diseased to the healthy eye. This is particularly probable where extensive acute inflammatory conditions exist in the infected eye. Here bacterial vaccines would no doubt be of inestimable value in limiting the infective process to the involved eye.

I treated a man who, while cutting the wire on a bale of hay, was struck by the end of the wire in the sclera at the

corneal margin, the eyeball being penetrated. The eye received no medical attention for several days and when I saw it there was extensive infection producing a panophthalmia with much pain and swelling extending to the orbit. The seriousness of the situation was recognized, but wishing to give him the benefit of the doubt a combined streptococcus-staphylococcus vaccine was given at once. Local treatment consisted of ice-cloth applications. One day after giving the vaccine the pain and swelling began to subside. I made four inoculations of the same vaccine at four-day intervals with the result that there was practically no pain during all this time, the patient being able to sleep at night without resorting to narcotics. The eye, however, showed complete disorganization and I advised enucleation, which I performed. On opening the eye-ball, after removing it, the interior was filled with pus and what interested me particularly was the slight amount of disturbance as found from the condition of the eye. To my mind this was conclusive evidence that the immunizing effect of the vaccines was responsible for this favorable condition. Such experience would naturally lead one to believe that vaccines would be potent remedies in avoiding sympathetic ophthalmia.

The ophthalmological annals of the past few years are crowded with contributions to the literature of vaccine therapy. A few of the most striking ones are given in the following pages.

EXTRACTS FROM CURRENT LITERATURE.

Leon S. Medalia (Boston Medical and Surgical Journal, Oct. 22, 1914), in his paper on vaccine treatment in eye diseases of bacterial origin, briefly reviews the literature on this subject as follows:

"Stephen Mayou[2] reported 30 cases of styes treated by him with vaccines with uniform success. All of his cases

[2] Mayou, Stephen: "Serum and Vaccine Therapy in Connection with Diseases of the Eye." Ann. Ophthal., St. Louis, 1912, vol. xxi, pp. 669-734.

had at least three attacks of styes while some had as many as twenty. In all cases local treatment did not prevent recurrence. The staphylococcus albus was present in all but seven cases. In the latter staphylococcus aureus was present, causing a much more severe condition. Out of ten cases of multiple and recurrent chalazions which he treated by vaccines eight recovered and showed no fresh chalazions after first treatment; the other two improved. He also treated four cases of severe purulent corneal ulceration due to staphylococcus with 'very satisfactory results in every case.' Thirty-six hours after first injection there was no spreading of the ulcers in any of his cases. In one case there was paralysis of the fifth nerve, cornea insensitive;—ulcer healed in two weeks as if no trophic disturbance of the cornea existed. One case of acute non-suppurative uveitis due to staphylococcus apparently secondary to boils recovered by the use of autogenous vaccine made up from the boils. The hypopyon was gone after the first treatment.

"He used gonococcus vaccine in two cases of gonorrheal rheumatic iritis. In one case there was no recurrence for a year, while in the other where the vaccine was used for gonorrheal rheumatism an attack of iritis developed three weeks after third inoculation. (He apparently used too small doses—25 to 50 million.)

"Mayou[2] also cites 30 cases of chronic non-suppurative uveitis of endogenous origin, fifteen tuberculous, ten staphylococcal and five syphilitic. The fifteen cases of tuberculous uveitis he treated with tuberculin. In twelve the eyes became quiescent; the amount of vision regained depended upon the stage of the disease when the treatment was begun. The other three cases were not benefited.

"I may mention here the good results reported by Derby[3] in the 30 cases of tubercular infection of the uveal tract which he treated with tuberculin.

"In the ten cases of uveitis of staphylococcus origin Mayou[2] used a staphylococcus autogenous vaccine with very good results. He obtained the autogenous vaccine by performing an initial paracentesis. He also resorted to

[3] Derby: "Vaccine and Serum Therapy in Ocular Tuberculosis." Trans. Amer. Ophthal. Soc., 1910, p. 614.

repeated paracentesis in addition to the vaccine treatment in these cases as a therapeutic measure. He reports two cases of cataract pre-operative immunization in which staphylococcus and Morax-Axenfeld bacillus were present in large numbers and could not be gotten rid of after six weeks of local treatment. He used mixed vaccines; the operation was performed. No inflammation intervened. In a case of subacute glaucoma with a mixed staphylococcus and pneumococcus infection he administered a mixed vaccine two days previous to the operation and no inflammation supervened.

"He also cites a case of post-cataract infection in an old woman of 89 treated by vaccines and a control case of a similar infection in a younger robust individual treated in the ordinary way without vaccines. He concluded that the final results in the more unfavorable case treated by vaccines 'was far better than the control case,' which he thinks can be attributed only to its use.

"Non-suppurative uveitis following wound infection (post-operative) which is as a rule responsible for sympathetic ophthalmia, Mayou considers as being due to a mildly virulent organism such as staphylococcus. He reports ten such cases of cyclitis with keratitis punctata which he treated by vaccine. In five cases in the early stage of the disease the condition cleared up after four treatments at an interval of two weeks. The other five cases had the treatment extended for three months, but they all ultimately cleared up. In none of these ten cases did cyclitis occur. In five of the cases he says there was no doubt of the beneficial effect of the treatment since they showed improvement in vision at the second or third day after the injection which lasted to the tenth day and then commenced to be misty again.

"Vandergrift[4] reports one case of gonorrheal choroiditis (chorioretinitis) with severe hyalitis, treated by staphylococcus and gonococcus vaccines successfully.

"Bryan[5] reports one case of very chronic lachrymal sac

[4] Vandergrift, G. W.: "Successful Treatment of Gonorrheal Choroiditis by Vaccine" Jour. Am. Med Asso., Chicago, June 8, 1912.

[5] Bryan, C. W. G.: "Serum and Vaccine Therapy in Connection with Diseases of the Eye" British Med. Jour., March 16 and 23, 1912.

inflammation of two years' standing, due to the pneumococcus, which was cured by vaccine in two months. In acute gonorrheal conjunctivitis Bryan considers the vaccine of great value. He treated two severe cases. In one the condition cleared up in ten days—the other showed no apparent benefit, while in three cases of ophthalmia of the new-born the disease was cured in each case with no infection of the cornea. Bryan[5] also reports one case of late post-operative infection by streptococcus with intense chemosis—edges of the incision edematous, iris discolored, with hypopyon. Autogenous vaccine was made and administered. The inflammation gradually subsided and the eye became quiet in five weeks. Extraction and needling performed later without complication and vision 6/9 obtained.

"Rubrecht[6] reports a case of systemic gonorrhea with conjunctivitis and keratitis in which three doses of gonococcus vaccine were given with excellent results. He reports one case of chronic conjunctivitis due to Morax diplobacillus of ten years' duration treated by an autogenous vaccine for five months with marked improvement.

"Maddox[7] reports a case of wound infection following cataract operation in which the vitreous was gray and turbid, the iris rotten looking. The administration of staphylococcus vaccine was followed by rapid improvement and cure.

"De Schweinitz[8] reports a case of streptococcus hypopyon ulcer treated by vaccine which was followed by recovery."

In this paper Medalia gives a detailed report of a large series of cases of eye infections. His method consists in using a stock vaccine while an autogenous vaccine is being prepared. A few of his cases will illustrate what can be accomplished by this method:

"One other of my early cases of this group is a case I had with Dr. Easton.

"G. E., female, 66 years. Operated O. D. for senile

[6] Rubrecht Bull, de la Soc. Belge. d'Ophthal., 27, 1909, p. 82.
[7] Maddox Ophthalmoscope, June 1908.
[8] De Schweinitz. Therapeutic Gazette, Oct. 15, 1910.

cataract May 2, 1908. Everything went smoothly until eight days later (May 10), at which time the eye began to redden. (Was thought to be due to irritation of lower lid entropion coming on from bandaging.) On the 12th of May she showed edema of conjunctiva and small hypopyon. When all measures had failed and the case was growing from bad to worse I was called in to 'try the vaccines.' The staphylococcus opsonic index was .44 and the pneumococcus was .56. Cultures showed a pure growth of staphylococcus aureus. I gave her on the same day (May 12, 1908) 250,000,000 staphylococcus aureus and 50,000,000 pneumococcus stock vaccines. Little local reaction followed. The next day she received 500,000,000 autogenous staphylococcus vaccine. She received five more treatments at from two to three-day intervals and was discharged twelve days later (May 24) with 'perfect recovery.' Improvement was noticed within 24 to 36 hours following the first injection and progressed rapidly thereafter. May 24 there was no edema present. The spongy exudate which had filled the anterior chamber so that the iris could not be seen rapidly diminished along with the inflammation, leaving a thick membrane filling the pupil. Secondary operation resulted in vision O. D. 20/20 with + 14 sphere. (I am indebted to Dr. Easton for the clinical record of this and another case of hypopyon ulcer to be cited later.)

"G. W. E., male, 52 years. (Case 20) entered Massachusetts Charitable Eye and Ear Infirmary Feb. 17, 1913.

"Left eye had been inflamed for about four days. No injury. Examination showed conjunctiva and lids injected. Eye red. Central ulcer on cornea. Hypopyon. Iris slightly dull. Pupil moderate and reacts slowly. Faint fundus reflex. Tension moderate. Vision, fingers at two feet.

"The eye showed no improvement under ordinary measures. The hypopyon increased and the eye was growing worse. Vaccine treatment was begun Feb. 27 and was continued on an average of once every two to five days until April 15. (Had twelve treatments in seven weeks.) Smears and cultures showed a predominating streptococcus and a few pneumococci. March 4 a Saemish operation was performed. Pus reappeared in anterior chamber on March 8. On March 12 the hypopyon began to disappear. Injec-

tion decreased rapidly. April 15 the eye was whitening and the corneal scar was not noticeable. Was discharged cured April 15. Vision, 20/200.

"The outcome of this case is worth calling attention to because of the nature of the infection (streptococcus and pneumococcus). The character of the infection and the length of time elapsed before vaccine treatment was begun are, I believe, both responsible for the length of time it took this patient to recover.

"One case of muco-purulent conjunctivitis of eighteen years' duration. Tried many treatments with various eye specialists with no relief. Has been under the care of her present eye specialist for the last four years, who sent her in for vaccine treatment. The following is a brief record of her case:

"H. A. B., female, 40 years. Jan. 25, 1913, complained of having had a purulent discharge for the last eighteen years. No relief from any of the various local treatments used. Cultures showed a pure growth of staphylococcus aureus. Autogenous vaccine was made up. Treatment began Jan. 27 and continued on an average of once a week until April 16. She had another treatment on June 7, when she was discharged cured. She had nineteen treatments in all. After the third inoculation she showed marked improvement. Eye stopped discharging entirely three and one-half months after the vaccine treatment was begun. No recurrence of trouble to date—fourteen months.

"I had three cases referred to me for prophylactic treatment preliminary to cataract operations. One, a woman of 83 years (W. S. B.) referred by Dr. Standish for prophylactic treatment. Three years previous she had cataract removed O. D., which became infected. Panophthalmitis set in and the eye was enucleated. She returned May 5, 1911, for a Noyes operation on left eye. Discharge from orbit of right eye and conjunctival sac of left eye present.

"Cultures showed staphylococcus aureus and B. xerosis. The opsonic index was, staphylococcus .69, streptococcus 1.01, pneumococcus .90. She was given autogenous vaccine, receiving eight treatments in all at intervals of two to three days. Cultures two days prior to operation were

found to contain only two colonies of staphylococcus albus. The discharge from the eye to be operated upon had almost entirely ceased. Operation, June 2, followed by recovery without incident.

"In the other two cases cultures from the discharge of the eyes to be operated upon both showed staphylococcus, weak aureus and B. xerosis. One had three treatments of autogenous vaccine at an interval of two or four days and the other had one treatment before the operation. Cultures of both cases taken two days prior to operation were found sterile. Cataract operation in both was followed by uneventful recovery.

"While nothing definite can be said about the last two cases, in the first case of this group, however, both Dr. Standish and I have felt that the vaccine had been of great help in the final outcome of this case."

Medalia's conclusions are as follows:

"1. The use of vaccine in bacterial infections of the eye, if judiciously carried out, will yield results such as could not be obtained with any other method of treatment heretofore known.

"2. Autogenous vaccine should be used as soon as possible.

"3. In order to obtain good results optically as well, the vaccine treatment should be employed before permanent damage to the eye occurs.

"4. When used in infections of the anterior chamber, especially in hypopyon ulcers, repeated paracentesis, if performed in connection with vaccine treatment, will yield better results than when vaccine is used alone.

"5. Small and oft-repeated doses will do away with marked negative phases and minimize the chance of a possible set back, both of which might occur if too big a dose is employed.

"6. Vaccine if used in a prophylactic way is of value in connection with preoperative immunization. It is of special value in cataract operations where the conjunctiva

contains bacteria that cannot be gotten rid of in the ordinary way.

"7. The bacteriological examination in connection with prophylactic immunization of all cases prior to cataract operations seems to me to be the logical method of procedure and will do away, to a great extent, with running the risk of post-operative infections.

"In conclusion I wish to thank the entire staff of the Massachusetts Charitable Eye and Ear Infirmary for referring the cases to me and for their painstaking observations of the cases before, during, and after the vaccine treatment. I feel that I am especially indebted to Drs. Chandler, Standish and Easton, who were the first to give me the opportunity to study this method of treatment in diseases of the eye and for their helpful and valuable assistance throughout this work."

Dr. Don M. Campbell, of Detroit, (Bacterial Therapist, January, 1913) reports the following interesting cases of eye infection:

"Case 1. Infection of Corneal Wound After Cataract Operation.—J. J. B., aet. 59. Male, well nourished, presented himself for examination of his eyes on Oct. 17, 1906. The history was that he had suffered a gradual depreciation of sight in the left eye for two or three years. Examination revealed a mature senile cataract in this eye. On Oct. 18, 1906, in Harper Hospital, under all aseptic precautions, a smooth, successful extraction of his cataract was done by the combined method.

"On Oct. 19, when the dressings were removed (the patient having suffered considerable pain during the night before) the lids were found swollen and reddened, there was marked chemosis and the corneal wound was found open and the edges grav and infiltrated. Iris was present, the cornea steamy and the aqua was turpid. Eye extremely painful and sensitive to light. Vision was reduced to barely light perception.

"There was here undoubtedly, a septic infection of the corneal wound, an extremely dangerous condition and one which in my experience heretofore had invariably termi-

nated in the complete loss of the eye by panophthalmitis. However, in this case he was immediately given a full dose of a mixed stock vaccine and a culture made from the lips of the corneal wound; from this culture, which proved to be a streptococcus, an autogenous vaccine was made and full dose given at intervals of five days.

"In four weeks he left the hospital with the wound well closed and the septic process thoroughly under control.

"In three months, with the proper correction, his visual acuity was 6/10 of normal.

"At the present time this man has returned for readjustment of his glasses and now, six years after the operation, he has a visual acuity of 6/6, or fully normal, and reads Jaeger No. 1 readily—a truly marvelous result after such an infection. This experience has not been an isolated one, two other such infections after cataract extraction yielding quite as well to the same line of treatment.

"Case 2. Sympathetic Ophthalmia Following Wound of Eye.—Mr. K., aet. 19 years, wound in the eyeball six months before coming under observation. The wound had been produced by a piece of steel.

"The wounded eye was shrunken and sensitive to pressure. The sympathizing eye had been inflamed for four months and there was only preception to light or large objects. A typical sympathetic irido cyclitis.

"The stump was enucleated and the patient placed on vaccine injection, a mixed stock vaccine being used. All evidence of inflammatory action has subsided and his vision is 6/60 plus."

William A. Mann (The Bacterial Therapist, September, 1915) briefly reviews his experiences in a paper read before the Chicago Ophthalmological Society, April 21, 1913:

"In March, 1910, I presented a few notes on Vaccine in Eye Diseases' to the Wilmette Physicians' Club, and in April, 1910, I read a paper before the Evanston Branch of the Chicago Medical Society. These papers were based on two years' experience with private cases only.

"Cases were reported of phlyctenular keratitis, corneal ulcers, nonspecific iritis, choroiditis and uveitis and penetrating wounds of the eyeball. My conclusions then were that in the diseases mentioned a mixed vaccine of staphylococcus and streptococcus was of decided benefit. At this time, three years later, I feel still more confidence in the use of mixed vaccine in the diseases mentioned.

"In most of these diseases, those due to endogenous infection, it is hardly feasible to obtain a culture and grow an autogenous vaccine, so as a rule a mixture of strep. pyogenes and staph albus and aureus was used. In some of these cases the offending germ could be obtained by a paracentesis.

"Phlyctenular Conjunctivitis: Improvement rapid, and seldom a return of trouble or formation of new phlyctenulas.

"Phlyctenular Keratitis: Healing of ulcers hastened, but most decided results in the chronic type, where the ulcer has been imperfectly healed with recurring attacks of irritation. One injection usually would clear away all congestion in a few days; a second injection a week later was usually given. In one or two cases of marked tubercular type the improvement was not so rapid or permanent, but in no case was there a failure to improve after vaccine. In obstinate cases tuberculin in addition would be advised.

"Episcleritis: Inflammatory signs disappeared after one or two injections in nearly all cases.

"Iritis, Non-Specific: A number of cases have been treated and the regular course of the disease shortened. If given in early stage, pain is increased for 12 to 18 hours, and then usually improvement sets in. In one or two cases the disease was apparently absorbed, but usually is only shortened. In subacute or chronic conditions, I have not noted much increase in pain, but it may occur, and should be expected and planned for.

"Choroiditis: So few cases with acute choroiditis have been treated that I am not sure how much benefit has been derived from the vaccines, but in none of the few cases treated was there any extension.

"Uveitis: Improvement in all cases but one, and in this case pain was increased for 24 hours and patient did not return. Usually congestion lessens in 48 to 60 hours.

"Vitreous Opacities and deposits on Descemet's membrane are not particularly affected.

"These diseases are due to endogenous infection, and somewhere else in the body there is a focus of infection. It may be in the intestines, nasal sinuses, mouth (pyorrhea or tonsils), vagina, gall-bladder or one of numerous other places. As to the germ, the staphylococcus seem to be present in most cases, according to Mayou* of London. He made a paracentesis and inoculated culture media.

"In cases of suspected tuberculosis and in several where T. B. glands were present, in phlyctenular keratitis, improvement was not quite so rapid as in uncomplicated cases, but was always satisfactory and no tuberculin was used. It is a question whether the phlyctenule is not due partially or entirely to secondary infection, which is nearly always present, and not to tubercular infection alone.

"As preventive treatment, I have used this vaccine in traumatic and operative cases. In cataract operations, particularly rheumatic patients, I believe it will lessen the chances of infection, and iritis. In perforating injuries, it should lessen the results of infection, but does not always prevent cyclitis.

"Dosage: The adult dose is 30 000 000 strep. py. and 100.000.000 each Staph. Albus and Aureus (Sherman's No. 10). A smaller dose should be given to women and a proportionate dose for children. The reaction for a proper dose is entirely local. Some redness or soreness about the seat of injection. Doses are given every three to five days. The dose is increased gradually, and twice the original amount can be given in most cases after two or three injections. The injection is given subcutaneously in forearm or outer part of upper arm or in leg, back or chest. Occasionally, the average dose will cause a severe redness and swelling, in fact, all the appearance of a severe infection, but I have never seen any that suppurated. The fresher the

*Stephen Mayou, Annals of Ophthalmology, October, 1912.

vaccine the more reaction there is, and while all vaccines are dated, I find that towards the end of the period, a larger dose should be given. The preservative added usually causes considerable smarting, and I frequently add a minim or two of a two per cent cocaine sol. which lessens the burning. The treatment by vaccines need not interfere with any other treatment, and in fact the cause, if found, should be of course removed.

"Conclusions: A mixed vaccine of streptococcus and staphylococcus is of decided benefit in endogenous non-syphilitic infection of the eye (excluding metastatic choroiditis).

"In exogenous infection its benefits are much less apparent when the infection results in presence of pus, but have a beneficial effect."

Dr. Don. A. Vanderhoof (Illinois Medical Journal, December, 1909) reports a few interesting cases:

"On June 8, H. D. R., a barber by trade, came to the office for eye treatment. His trouble dated back five days, and, although under treatment by a physician, his condition had grown steadily worse. The eye had pained considerable ever since the trouble started; there had also been considerable lachrymation and photophobia.

"The day he came to the office he was complaining of considerable pain, both in the right eye and also on that side of his head. Both the upper and lower lids were swollen, and there was deep corneal congestion. Pupil small and round. The tension of the eye was +1 and the patient complained of a great deal of tenderness during the examination. I used scopolamin in the eye and kept him in the office for about three hours. The tension soon became less, but the pupil dilated very irregular indeed. A few drops of dionin, 2.5 per cent solution, was also used. He was directed to return home, to use hot applications and remain in a dark room. A laxative was also prescribed.

"June 9, pupil was still very irregular, and resisted all attempts to dilate it fully. Pain was severe at times. Same treatment was continued as previously given. June 10 at 3 o'clock a. m. he was taken with terrific pains in that eye

and through the right side of the head. Hot applications were applied and a cantharides blister used over right temple. Morphine sulphate one-fourth of a grain was given hypodermatically. Tension was +1 all that day so ordered a solution of dionin, cocaine and atropin, to be used every two hours during the day.

"As there was no change in his condition that evening I gave him an injection of streptococcus vaccine 30,000,000, which is prepared by G. H. Sherman, of Detroit, Mich. June 12 he rested very well during the night, excepting between 4 and 6 o'clock a. m., when he had considerable pain. I saw him about 5 o'clock a. m. Found the tension normal, eyelids much less inflamed and the pericorneal injection somewhat less. No pain on pressure this afternoon for the first time. Pupil still very irregular.

"From this time on he gained very rapidly, and in a few days he was back at his work against my wishes. A couple of days after his starting to work the eye became much worse, but I at once gave him another injection of the streptococcus vaccine. The iritis immediately quieted down and has caused no trouble since.

"Case 2. Mr. W. F. D., 30 years of age, came to the office on June 2, saying that for five days he had been having considerable pain and lachrymation in his left eye. He had done nothing for it up to the present time. The case I diagnosed as one of simple iritis, and, as it had been troubling him for a few days before requesting treatment, I advised absolute quiet in a dark room, using scopolamin, dionin and hot compresses, besides advising him to pay strict attention to his elimination.

"The symptoms of iritis were all present here, so I will not enumerate them. Up to June 11 there had been some improvement. Pain at night had almost disappeared. On June 12 I gave him an injection of streptococcus vaccine 30,000,000. The next afternoon quite a change for the better could be seen. The pericorneal injection was less intense, and he could now open his eye just a little for the first time in a number of days. The case from this time on recovered rapidly. Nothing new developed and only one injection of vaccine was used."

Dr. E. B. Cornell (Journal of the Michigan State Medical Association, October, 1912) reports, among other cases, the following cases of iritis:

"Case 1. R. G., 20 years of age, rheumatic iritis. Is driver of mail wagon. The attack occurred during cold weather. He refused to quit work. I prescribed the usual remedies, both locally and constitutionally. The disease remained about stationary—sometimes apparently a little improved, then the reverse. After several weeks the patient was exposed to a severe snow storm and the eye became much more painful. At this juncture I gave him the first dose of vaccine without much expectation of success. Within 48 hours, the pain subsided and the eye was decidedly improved; four days later another injection was given and the patient made a rapid recovery without losing a day from his occupation.

"Case 2. Mrs. E., 72 years of age. Rheumatic iritis, corneal ulcer and severe blepharospasm. Has been treated for many weeks without amelioration of symptoms. She had been afflicted with rheumatism for many years. Her finger joints were enlarged from this disease. Cocain, novocain, acoin, dionin and other medication would give but temporary relief. The first dose of vaccine gave some improvement and in ten days she became fairly comfortable. The injections were repeated every five days for several weeks. Not only were all her symptoms relieved, but the condition of rheumatic joints was vastly improved.

"Case 3. D. T., 45 years of age. Rheumatic iritis. This patient had previously had similar attacks and had been treated by other oculists. It usually required several weeks to overcome an attack. In 1909 he had an attack with the usual course. In 1911 the same conditions prevailed, but all symptoms were aborted by one vaccine injection.

"In many other cases which I have treated during the last two years, the relief from all painful symptoms within 24 hours, where rheumatism was a factor, was little short of marvelous."

Gonorrheal Iritis.

In gonorrheal iritis gonococcus vaccine should be used. Dr. John E. Weeks (Congress of American Physicians and Surgeons, 1910, p. 73) reports two cases of gonorrheal iritis successfully treated with gonococcus vaccine.

In this connection it is well to consider that in cases of iritis where the patient has gonorrhea it does not necessarily follow that the iritis is gonorrheal. Streptococcus infections may just as well be present in these cases, so if no good results should be obtained with gonococcus vaccines in these cases it is fair to presume that a streptococcus infection is present and a corresponding vaccine should be used.

Dr. W. K. Mittendorf (Medical Record, March, 1913) reports a series of cases of gonorrheal eye infections treated with gonococcus vaccine. The cases are typical in showing the results that are being obtained and the following are illustrative cases:

"Case1. Max N., age 24. Lids and ocular conjunctiva red and swollen and much pus. Had gonorrhea and rheumatism of the knee and pains in hip. Smears were negative from each eye, but cultures made grew gonococci; after three days the smears from the eyes were positive and there was a beginning involvement of the right cornea with some haziness. This case was undoubtedly a metastatic condition. Put in hospital, and gonococcus vaccine injected by hypodermic syringe, with argyrol, 25 per cent and boric acid irrigation locally. Previous to admission he had had this treatment but steadily grew worse. The vaccine injections were given every third day—first 50 000,000 gonococcus and 200,000,000 staphylococcus albus, the other doses double this amount. In 48 hours the swelling was gone in the lids and the eyeballs were almost white. The case steadily improved and the smears were negative in two weeks. The patient was held a week and discharged in three weeks with eyes well. The rheumatism had also disappeared. Two weeks later he reported he was again

working as a butcher carrying heavy meats and on his feet all day with perfect comfort.

"Case 2. Baby F., age three days; premature baby seven months. Both eyes were badly swollen and red, discharging much pus; had been using argyrol, 20 per cent, but eyes got much worse. Smears showed numerous gonococci. Baby small and weak and would take no nourishment. It was in the country and could not go to hospital so I decided to use vaccine of gonococci 50,000,000, pseudo Klebs-Loeffler 50,000 000, staphylococcus albus 100,000,000, streptococcus 50,000,000, colon bacillus 50,000 000. The first dose was one-third of this amount and the subsequent doses (at two-day intervals) one-half. After the second day the swelling in the left eye had disappeared and the baby was feeling better and took some nourishment. After the fourth day both eyes had lost all swelling and there was very little discharge. The next three days baby had almost no local treatment as the mother developed pleurisy and could not attend to it, but it lost no ground and opened both eyes nicely. In two weeks the eyes were cured and the vaccine was discontinued with only occasional local treatment. This baby was nourished hardly at all and was very weak during the whole course of treatment, but was not affected in any way by the vaccine injections and lived for seven weeks before it died of malnutrition on the approach of cold weather. The physician attending the family had not expected the child to live a week when it was born.

"Case 3. Baby Wm. D., age 15 months. Had sore eyes about a week when taken to hospital. Both eyes were swollen and outside of lids very red and closed tight. Treated three days in hospital; no improvement. Same vaccine used as in preceding case in same dosage. On the second day after injection the baby opened both eyes, the swelling was almost gone, and the discharge was very limited. Vaccine was used at three-day intervals during the second week. Both eyes were closed again for one day and a small ulcer was discovered on the left cornea, but this was yellowish and raised, with no haziness of the cornea except in the limited area of the ulcer. Atropine ordered t.i.d. Two days later the ulcer appeared the same, but smears from both eyes were negative. As ulcer appeared phlyctenular, I applied yellow oxide of mercury, gr. i, in lanolina 3iss, morning

and night. The ulcer began to improve immediately and in 48 hours was healed. After six injections the patient was discharged cured.

"Case 4. John H., age 20 years. Old extensive macula in the right cornea from traumatism. He had posterior urethritis and rheumatism of knee, finger and elbow. Both eyes were red and lids somewhat swollen with much discharge. Argyrol and boric acid irrigation was ordered, and a vaccine of 100,000,000 gonococcus and 80,000,000 staphylococcus albus were injected every three days. There was immediate improvement in both eyes. On the sixth day he had pain in the right eye and some redness—probably iritis irritation—as there was no ulcer on the cornea; this disappeared the next day. After six injections the patient was discharged, both eyes showing negative smears. After eighteen days treatment the rheumatism was almost gone. After the patient had gone home his physician gave him a very large dose of vaccine, estimated at 250,000,000, but probably more. In 48 hours both eyes were red, all the joints were inflamed, and small ring of ulcers appeared on the left cornea. Smears were negative in both eyes. He was sent to the ward, atropine was used, and a vaccine of 100,000,000 gonococci was given. In three days the eyes and joints were better, and two days later the patient was discharged and walked out of hospital without a cane. Ten days later he reported all well in both eyes. He had danced all the preceding evening without any inconvenience at all."

CHAPTER XII.

INFECTIONS OF THE DIGESTIVE TRACT AND ABDOMINAL VISCERA.

Digestive Disturbances

Digestive disturbance is one of the prominent clinical symptoms of infectious processes in any part of the body, and this disturbance is as a rule in direct proportion to the acuteness and extent of the infection. In generalized acute infections, digestive disturbances are more pronounced than in localized chronic bacterial invasions. If a chronic infection, however, directly involves the digestive organs, proportionately much more pronounced disturbances of the digestive functions take place.

Extensive bacterial examinations of inflamed or ulcerated tissues of the abdominal viscera, from specimens procured in abdominal surgery, show that the principal infecting organisms are the colon bacillus, the streptococcus, the pneumococcus, and the staphylococcus. Of these the streptococcus appears to be the most persistently pathogenic and in many localized infections of the digestive tract it is a question whether the focus of infection developed from the presence of the streptococcus in the blood or from swallowing the organism. Colon bacilli are generally associated with suppurating processes, and are frequently accompanied by other organisms. Mixed infections are common in which two or more of the principal micro-organisms are present. From this it is clear that, when confronted with inflammatory disturbances due to infections of the abdominal organs, it is always advisable to consider one or more of these organisms the probable cause of the infection, unless it can be demonstrated that some specific infection, like typhoid or tuberculosis, exists. Not being in a position to definitely determine what the infecting organisms are, it is more practical to give a vaccine containing the four chief organisms—colon bacillus, streptococcus, pneumococcus and staphylococcus, than to postpone vaccine treatment until a more definite bacterial diagnosis can be made.

The advantages of employing vaccine in digestive disturbances was first impressed on my mind when I saw the beneficial tonic influence they had on the digestive organs, while treating cases of chronic rheumatism with vaccines. This tonic influence was also observed when vaccines were given for bronchitis, "colds" and other troubles. Here I can speak from personal experience, having myself taken vaccines for "colds" with which I formerly was greatly annoyed. The injection of a vaccine in this condition is followed by an improvement in appetite which stimulates to eating between meal times, and the digestion is equally good.

Such experiences suggested the idea of using vaccines in cases of indigestion where the trouble could not be ascribed to any organic cause.

The proper attention to digestive disturbances is a very important factor in every-day practice. There is probably no organ of the body more abused than the stomach, and it is not unreasonable to suppose that the rest of the intestinal tract may become involved. Where dietetic and other abuses are continued it would be useless to expect relief from the vaccine treatment. The dilated stomach of the excessive beer drinker, the irritated stomach of the alcoholic, impaired digestion from improper food and over-eating are all conditions that require special attention, but diseased conditions due to the invasion of infective organisms following digestive abuses must also be considered important in the treatment of these cases. If an infection has once taken place as a consequence of a prolonged debauch it does not necessarily follow that the infection will voluntarily subside later, when proper living is resumed.

The proper function of the liver is an important factor in digestion as well as in the process of assimilation. Irritating substances absorbed from the digestive tract and circulated through the liver by the portal vein no doubt predispose to infective processes of the liver. Excessive use of alcohol has long been recognized as an etiologic factor in cirrhosis

of the liver. Experiments on lower animals, however, show that the irritant itself does not necessarily produce the disease but simply creates a condition favorable for infections by pathogenic organisms which complete the chain in the disease process. This is aptly pointed out in an editorial in the Journal A. M. A., Jan. 21, 1911, page 200 from which I will quote as follows:

"E. L. Opie in his experiments has shown that bacteria in association with toxic substances having a special affinity for the liver, such as chloroform and phosphorus, may produce changes which neither the poison nor the bacteria can cause when acting alone. The possibility that disturbances of metabolism in man may produce changes in the liver similar to those caused by such poisons is well illustrated by the toxemia of pregnancy, in which persistent vomiting is associated with central necrosis of the hepatic lobule similar to that caused by chloroform. The experiments show that the activity of the hepatic poison may be so intensified by bacterial infection that a quantity of the poison which alone produces little change, may in combination with bacillus coli and streptococcus pyogenes, cause destruction of almost the entire hepatic parenchyma. Some bacteria (e. g., colon bacilli), which have little pathogenicity for the normal animal are virulent for the animal whose liver has been injured by chloroform or phosphorus. It is possible that those instances of acute yellow atrophy which accompany infection with streptococcus pyogenes are dependent on some disturbances of metabolism or other form of intoxication which has rendered the liver unusually susceptible.

"The experiments, furthermore, show that bacterial infection can influence and even determine the development of cirrhosis of the liver. Degenerative changes which usually undergo rapid repair may cause sclerosis when combined with bacterial infection. Whereas cirrhosis may be caused by chloroform without bacterial inoculation, the introduction of bacteria hastens the progress of the chronic change. The poison in large quantity rapidly causes death, but a much smaller quantity in association with a relatively non-pathogenic micro-organism produces a lesion from which recovery is possible. Such insults repeated at intervals produce the chronic changes of cirrhosis.

"This experimental work suggests the explanation of the fact that some alcoholics escape cirrhosis, while temperate persons and even total abstainers sometimes develop the disease. In the latter case we may assume that the toxic element of the etiologic combination arises from the production inside the body."

Cases of acute indigestion associated with diarrhea are almost invariably of bacterial origin and toxic material from this source circulating through the liver may cause sufficient irritation to start an infection. It is not an uncommon experience to have a catarrhal jaundice follow an attack of diarrhea. These hepatic catarrhs are no doubt due to infections which in all probability had their origin in an irritated condition due to toxic materials absorbed from the impaired digestive organs.

CATARRHAL JAUNDICE.

That these cases of acute catarrhal jaundice are due to infections is well illustrated by the marked beneficial results that are being obtained from bacterin inoculations. I fully realize that these cases recover spontaneously, sometimes within a week or two, but the rapid improvement that takes place after the first vaccine inoculation can only be ascribed to the vaccine. In my early experiences I employed a combined streptococcus and colon bacillus vaccine in five successive cases with uniformly good results. Inoculations were made from five to seven days apart. One case received but one dose, two were inoculated twice, one three times and one four times. More frequently I employed a combined stock vaccine containing colon bacilli 200,000,000, streptococci 100,000,000, pneumococci 100,000,000, and staphylococci aureus, albus, and citreus, each 200,000,000 per cubic centimeter, of which about 0.3 cc. was usually given as the initial dose, and treatment continued in gradually increasing doses as indicated. The results with this combined vaccine have been uniformly good.

Mild forms of infection may exist without producing the extreme symptoms observed in a case of jaundice. Infective processes are frequently seen where the contest between the tissue cells and the invading organism is so well balanced that the diseased condition remains about the same for months. This is especially true in milder forms of infection. In an alcoholic, during the early stages of cirrhosis of the liver we probably have a subdued infection following the wake of the alcoholic irritant. The same condition would hold good with cases of non-alcoholic cirrhosis where the hepatic irritant may have its origin in bacterial products absorbed from the alimentary tract during digestive disturbances.

With a raised immunizing resistance combined with the general tonic influence of vaccines much can be accomplished by this treatment in cases that are not amenable to ordinary methods. In digestive disturbances, the recognized general rules of proper dieting and bowel regulation should also be observed. The influence of vaccines in cases of constipation has often impressed me much. With an improved appetite and good digestion a surprising regularity of the bowels often follows without any other treatment.

On the question of diet I find that the amount of salt taken with the food has some relation to persistent hyperacidity of the stomach. Common salt being the source of the chlorine for the production of hydrochloric acid in the stomach, it occurred to me that by giving a salt-free diet in such cases the hyperacidity might be checked. Two years' experience with this method of handling these cases fully sustains my opinion. To get the benefit of the salt-free diet it must be kept up for three or four weeks.

I have used vaccines extensively in the direct treatment of digestive disturbances and feel that they should be uniformly applied in these cases. Where no malignant condition exists good results may nearly always be looked for.

I wish to cite two illustrative cases:

A young woman complained of having had trouble with her stomach for seven years. Had lost thirty pounds in weight and weighed only ninety-one pounds. Some tenderness on pressure over the stomach was noticed and also a slight pain over the right hip and back. She ate very sparingly and complained of distress and belching of gas after eating. The tongue was coated, bowels fairly regular, and she slept well. She had been treated by many physicians, but was steadily failing. She had been referred to me by one of my vertigo patients and naturally was prepared for the vaccine treatment.

I started to treat her with streptococcus and colon bacillus combination making inoculations at seven-day intervals. After the fourth inoculation she began to improve and the treatment was continued until she had had eight inoculations, then treatments were extended to fourteen-day intervals.

During the summer she went to the country for a few weeks and came back with a fever. I did not recognize the character of the fever at first but soon found it to be a typical case of malaria. Vigorous quinine treatment broke up the fever, but all she had gained from the vaccine treatment was lost.

About a month after she had recovered from the malaria, the vaccine treatment was started again. She soon began to improve and after receiving ten inoculations seemed to be entirely well. She has gained twelve pounds in weight, feels stronger, has no more distress after eating and in every way is better than she has been in many years.

A middle aged woman had been bothered with indigestion for three years. I treated her with tonics and other conventional remedies for two months with no benefit. She had tried other physicians with no better results. I was at that time treating her father for rheumatism and the suggestion of giving a vaccine for her dyspepsia was readily

accepted. She made a complete recovery after five inoculations of a streptococcus and colon bacillus vaccine. A year and a half later she had another attack of indigestion, for which the same vaccine treatment was employed. She began to improve after using the vaccine and after eight inoculations at five-day intervals made a complete recovery.

GASTRITIS.

Gastritis is so frequently associated with pyorrhea that the infective character of this ailment as a result of constant pus swallowing which is liberated from the teeth sockets is quite clear. The natural inference also is that the same pyogenic organisms that are responsible for the pus formation in pyorrhea are also causing the gastritis. That the streptococcus is a factor in chronic gastritis is entirely probable, and no doubt other pyogenic organisms, including the colon bacillus, are also responsible. The fact that over 80 per cent of cases of stomach cancer give a history of pyorrhea with chronic gastritis prior to cancer development establishes a close relationship between the primary pyorrheal mouth infections, gastritis, with its resulting chronic irritation, and the final cancer development from this irritation.

From this viewpoint, the importance of using vaccines in the treatment of gastritis is apparent. The same combined vaccine usually employed in the treatment of pyorrhea, with the addition of a colon bacilli, should be employed. Such a combined vaccine will be serviceable for the gastritis and pyorrhea at the same time. By building up an immunity of sufficient intensity to eliminate the gastritis and pyorrhea with vaccine inoculations the chronic irritation incidental to the infection will be disposed of and corresponding dangers of cancer development avoided.

GASTRIC ULCERS.

The etiology of gastric ulcers has been very carefully studied by Billings and Rosenau, especially in relation to

their bacterial flora. The method consisted in opening the abdomen and extirpating the ulcerated portion of the stomach and then carefully making cultures from the deeper structures of the ulcerated tissue, so as to avoid surface organisms as possible contaminating factors. These examinations show the streptococcus as the constant infecting agent in these cases. Furthermore, they found that if this streptococcus is cultured and injected intravenously into animals it has a particular tendency to localize in the stomach of the animal and cause gastric inflammation.

E. C. Rosenau (Journal A. M. A., Nov. 13, 1915, p. 1687) reports a large series of animal inoculations with streptococci isolated from various organs of the body and shows that streptococci isolated from a particular organ under diseased conditions in man, when cultured and injected intravenously into animals, produced localized infections in a large majority of cases in the organ corresponding to the one from which the germ was isolated. This was found to be most markedly the case when the cultures were fresh and had only been grown on culture media for a few days. To illustrate: Streptococci isolated from cases of appendicitis showed infections of the appendix in 68 per cent of the inoculated animals; streptococci isolated from cases of cholecystitis caused lesions in the gallbladder of 80 per cent; streptococci isolated from ulcers of the stomach in man caused lesions in the stomach and duodenum in 60 per cent; streptococci isolated in cases of erythema nodosum caused skin lesions in 90 per cent; streptococci isolated from cases of endocarditis showed infections of the endocardium in 84 per cent of the animals inoculated. The same experiments were carried out with streptococci isolated from other organs with similar results. His experiments also show that, if the streptococcus is grown on the usual culture media for a week or more, this "elective" tendency is to a large extent, if not entirely, lost. Thus, elective localization of infection took place in 76.4 per cent of the animals

referred to above, whereas the same series of experiments shows that where animals were inoculated with the same organisms, after they had been grown on culture media for a week or longer, elective localization of the infection took place in only 14 per cent of the animals. In the same article Dr. Rosenau refers to work done by Forssner in which he showed that when streptococci are grown in kidney and kidney extracts they acquire a special predilection for the kidney, when injected intravenously.

These experiments show that streptococci are particularly virulent for the tissues of organs that they have previously grown in. Virulence of an organism depends upon the effectiveness of its digestion and assimilating properties on the tissues where it succeeds in establishing itself and these experiments show that streptococci which have grown on certain tissues for some time have acquired the habit of more effectively digesting such tissues than tissues of other parts of the body, and consequently when injected intravenously are more able to maintain themselves in the tissues of organs that they have been accustomed to grow in than in other tissues. In other words, streptococci that have acquired the habit of living and growing on stomach tissues can attack stomach tissues more readily than other parts of the body; or, stomach tissues are less able to resist invasions of such an organism than other tissues of the body. These experiments also show that this faculty of streptococci to more readily attack organs or tissues of the same kind that they have previously lived or grown in is rapidly lost when they have grown on other substances for some generations. This shows that it is not so much the specific character of the organism that determines its elective character in attacking the stomach, gallbladder, appendix or some other organ, but that this faculty is acquired from the circumstance or condition under which it lives. This acquired ability of a streptococcus to more readily attack or maintain itself in certain tissues of the body also accounts

for the persistence of an infection in one organ or in a certain variety of tissues while other parts of the body remain free from infection. When a streptococcus has once acquired the habit of living on stomach tissues it may continue to maintain itself there while other parts of the body are quite able to resist invasion by this particular organism. The same would be true of a streptococcus cholecystitis or appendicitis. In a streptococcus joint infection, however, there being many joints, streptococci liberated from an involved joint may quickly attack another joint, as seen in cases of arthritis. These considerations have an important bearing on active immunization as a therapeutic measure. On first thought it would appear that from the acquired specificity of the organism specific antibodies produced by the tissues of the involved organ would be necessary to overcome the infection. It may seem that in an ulcerated stomach, for example, the antigenic properties of the infecting organisms would fit in more perfectly to produce the specific antibodies necessary for the destruction of the germ than any artificial means of injecting killed organisms into entirely different tissues of the body could be. But the fact that streptococcus infections of a given organ have a distinct tendency to run a prolonged course shows that the faculty of the germ to adapt itself so that it can live and grow in that particular tissue is as strong or stronger than its antigenic properties. Under such circumstances it is perfectly clear that, to overcome the infection, outside aid is necessary. In this connection it is important to realize that antibodies for the destruction of certain infecting organisms must not necessarily be produced by the activities of the tissue cells of the infected organ, but that other tissues of the body can also be called upon to actively produce antibodies to aid the diseased tissues in overcoming the infection. Subcutaneous injections of killed streptococci, by acting on the tissues under the skin, will be instrumental in the production of antibodies that will aid in

destroying the streptococci in a streptococcus keratitis, cholecystitis, or other streptococcus infections. This same principle holds good with other infections. A gonococcus vaccine when injected under the skin will aid in overcoming a gonorrheal arthritis, orchitis, or conjunctivitis.

All this clearly shows that it is not absolutely necessary to have a vaccine prepared from organisms that have been isolated from infections of the same kind of body tissue that is under treatment, but that therapeutic immunizing responses are aroused by the use of vaccines containing micro-organisms obtained from different sources. This fact is of special importance in the treatment of abdominal infections with vaccines because an exact bacterial diagnosis in infections of abdominal organs would require a surgical operation.

So in the treatment of gastric ulcers a vaccine containing polyvalent streptococci in combination with other organisms often found as complicating infectors constitutes an efficient therapeutic agent. The same combined vaccine, containing streptococci, colon bacilli, pneumococci and staphylococci, referred to in the treatment of catarrhal jaundice, also gives good service in gastric ulcers. Where the ulcers are of long standing or where the ulcers have caused hemorrhages the ulcers should be surgically removed and the vaccine employed to promote healing of the wound.

CHOLECYSTITIS.

Infections of the gallbladder are due mostly to streptococci and colon bacilli with staphylococci and pneumococci as the other principal invaders. In some cases the typhoid bacillus becomes a chronic infector. That gallstones are of secondary development, being due to and not the cause of infection, is now well established. This necessarily assumes that the infection in the gallbladder existed for considerable time before gallstones formed, because they develop slowly. Experience shows that drugs are of little

therapeutic value in the treatment of these cases before gallstones develop, and that where recoveries do take place it must be ascribed to the development of immunizing resistance to the germs causing the infection. Active immunization with the aid of bacterial vaccine offers a distinct therapeutic aid in the treatment of these cases. When treatment is started early, a cure can be secured in time to prevent gallstone formation. A combined vaccine containing streptococci, colon bacilli, pneumococci and staphylococci serves well and should be employed at five to seven-day intervals. In the early acute stages inoculations may be made to advantage two or three days apart.

Where the cholecystitis dates from an attack of typhoid fever, a possible typhoid infection should always be considered and if prompt improvement does not follow the use of the combined vaccine a typhoid vaccine should be employed and the case treated as a typhoid carrier.

Where gallstones are present they should be removed surgically, and taking cultures from scrapings of the gallbladder should not be neglected. These operative cases should be treated with stock vaccines before the operation, to build up an immunizing resistance, so as to avoid postoperative extensions of the infection; and after the operation the vaccine should be employed to effect a permanent cure. If unusual organisms are found in the cultures taken, an autogenous vaccine should be made up and employed.

INFECTIONS OF THE PANCREAS—DIABETES.

That inflammation of the pancreas is very closely associated with diabetes is now quite generally recognized, Max Einhorn (Journal A. M. A., July 10, 1915, p. 149) points out in a critical analysis on pancreatitis that Opie contends that the islands of Langerhans are diseased in 85 per cent of diabetes cases and that generally a diagnosis of chronic pancreatitis can be made out. Pancreatitis is also often associated with cholecystitis and infection of the bile ducts.

The close relationship of the islands of Langerhans located in the head of the pancreas, to the function of maintaining a sugar metabolism has been demonstrated by animal experimentation; so we can readily see that an inflammatory process in the pancreas is also liable to involve the islands of Langerhans.

Modern pathology through the study of bacteriology and infection has lead us to a point where we can hardly conceive of an inflamed organ without ascribing the condition to an infection. That a chronic infection by the common infecting organisms may develop in the pancreas as well as in the liver or other organs can not be doubted. If the contention that the islands of Langerhans are internal secreting organs and that they secrete a substance which controls sugar metabolism is correct, we can readily understand how an infection can disturb or even destroy their function with a resulting diabetes. From this viewpoint vaccines are most logical remedies to use in the treatment of diabetes, and the results so far obtained justifies this position.

The ultimate results from immuno-therapy when applied to restoring the functions of an organ depend largely on the amount of damage that the infection has done before immunization can be established. An infection of an eye, for example, may temporarily impair vision or if severe, permanently destroy the function of the organ. So, an infection of the islands of Langerhans or other organs that possess the function of secreting metabolic enzymes for the purpose of controlling sugar metabolism may be sufficient to impair their function temporarily until the infection is eliminated or, on the other hand, the infection may be sufficiently intense or prolonged to permanently destroy their function with no possible restoration even if the infection is overcome. Where the diabetes is of long standing, not much if any benefit from the use of vaccines should be

expected, because in such cases the infection has in all probability progressed to a permanent destruction of the special gland structure. On the other hand, if the disease is of comparatively recent date striking benefit from the immunizing influence may be expected. I will cite a few personal experiences:

Miss L. M., aged 24. I had treated this girl for diphtheria when she was five years old. Post diphtheritic paralysis set in with difficulty in swallowing. Death seemed imminent, but after a long illness she recovered. Her father was an alcoholic and died of tuberculosis when she was about two years of age. She began to work in a dress maker's shop while quite young, and never developed robust health. I frequently treated her for minor ailments from time to time, prior to her having diabetes. At this time she complained of being easily fatigued, thirsty and passing an unusual amount of urine. Examination of the urine showed a large amount of sugar. She was directed to quit working; was placed on a diabetic diet and 0.3 c.c. of a mixed vaccine containing streptococcus 100,000,000, pneumococcus 100,000,000, staphylococcus aureus, albus and citreus each 200,000,000 and colon bacillus 200,000,000 per c.c. was given. The vaccine was given at five-day intervals with gradually increasing doses. After four weeks' treatment the sugar had entirely disappeared from the urine. She soon regained her normal strength, disregarded my instructions to continue on a diabetic diet, and about eight months later got married. I took care of her a year later in a confinement. Outside of its being an instrumental delivery, everything progressed nicely. I kept track of her for about a year more and there was no return of the diabetes. I am satisfied that the diabetes in this case, though acute, had not been of long standing.

Mr. M., aged 50, married, with a large family of healthy children. Organist and music teacher. Had been suffering

for a few years with bronchitis which was steadily growing worse. Went to Germany during the summer of 1911, thinking the trip and treatment by a German physician would benefit him, but he got worse. On December 10, 1911, he called at my office. On examination I found extensive bronchitis in both lungs. He was anemic and said he had lost considerable in weight; he complained of being easily fatigued and was obliged to urinate two or three times during the night. Sputum examination showed no tubercle bacilli, but the usual pus cocci were present in great numbers. Urine examination showed a large amount of sugar. He said no one had made a urinary examination before this, so it is impossible to know of how long standing the diabetes was, but from his general appearance and symptoms of the case it must have existed for some months. A combined pneumococcus-streptococcus-staphylococcus-colon bacillus vaccine was given at five-day intervals, while at the same time rest and a diabetic diet was prescribed. The amount of sugar in the urine rapidly became less but did not entirely clear up. Four months later he developed an occipitol-frontal neuralgia which annoyed him for something over three months. The bronchitis cleared up rapidly after using the vaccine and in six weeks' time was entirely free from cough. He began to feel stronger and improved generally. The amount of sugar in the urine fluctuated, it sometimes being almost absent, then appearing again. After six months' vaccine treatment, the urine at times was entirely free from sugar. Treatment was continued at somewhat irregular intervals for a year more, at the end of which time the urine was entirely free from sugar. He was then advised to return slowly to a regular diet, but no more sugar was found in the urine. The last examination of the urine was made Dec. 14, 1915, after he had been on a regular diet for several years and no trace of sugar was found. He has entirely regained his former good health and feels happy.

A recent case will prove interesting. Mr. D., aged 56, a professional gentleman doing much writing and public speaking; had enjoyed the usual good health with the exception of occasional rheumatic pains until September, 1915, when he began to feel ill. He complained of peculiar pains in legs, chest and head. During October the condition grew worse and in a month's time he lost thirty pounds. He complained of a crushing feeling which made him feel as though he were loaded down with a heavy weight, as he explained it, and felt very weak. He had some difficulty in moving his left leg, and right foot felt numb. He noticed an increase of urine voided and found that it amounted to about eight pints in twenty-four hours.

On November ninth he consulted his family physician who made a diagnosis of diabetes, there being a high percentage of sugar present. The doctor prescribed a carefully selected diabetic diet and other conventional remedies usually employed in this disease. After four weeks' treatment he felt somewhat stronger but the percentage of sugar in the urine remained the same. There being no material improvement, he wished to try the vaccine treatment. His doctor insisted that I should give the vaccine while he continued the other treatment. A mixed vaccine containing colon bacillus, streptococcus, pneumococcus and staphylococcus was given at five day intervals. Treatment was started with the usual small dose and increased as indicated by the usual reactions. Improvement was soon observed after using the vaccine. He has now been under vaccine treatment for five months and is at the present time receiving vaccines at weekly intervals. The amount of sugar in the urine gradually decreased to occasional traces and during the last four weeks it has entirely disappeared although he eats six large slices of whole wheat bread every day in conjunction with raw eggs and some vegetables. He has a good appetite and digests his

food well. His general condition is such that from all appearances, he will regain his former vigorous health.

Another case was in a woman aged 45 years. Her case was of longer standing but not so aggravated, there being only a small amount of sugar present. She received in all 22 inoculations of the same combined vaccine at five-to seven-day intervals, when the urine was entirely cleared up. I have lost track of this case and consequently am unable to say whether or not she relapsed.

I have used vaccines on four advanced cases of diabetes without any benefit whatever.

Dr. James Miller, of Edinburgh (Journal of Vaccine Therapy, May, 1912, London) reports some interesting experiences as follows:

"W. B. —, a farmer, aged 60 years, a patient of Dr. Davidson of Busby, was first seen in this illness by his medical attendant on May 9th, 1909. He was suffering from a carbuncle on the nape of the neck. His previous health had been excellent with the exception of two attacks of erysipelas several years ago, the first lasting for three months, the second a few days. When seen on May 9th, the patient had been feeling ill for three or four days, but had not been keeping indoors. On the nape of the neck was a carbuncle with extensive and deep in filtration of the surrounding tissues. During the ensuing weeks there was a very free purulent discharge, so copious that the dressings had to be changed every two hours. Then infiltration extended across the back of the neck as far as the left ear while the glands in the right posterior triangle became enlarged and painful. Sloughs were removed from the low, large abscess-cavity, while a furunculosis of the neighboring skin supervened. Heart and lungs were normal at this period, and it was stated that the urine gave no abnormal reaction.

"On June 4th, two right lower molars which had been causing ulceration of the tongue were removed. On June 10th, the patient consented to have vaccine treatment, and on this date I saw him. He looked very ill indeed. The temperature was 103 degrees F., and the pulse-rate, 120; the

whole of the face and ears were deeply cyanosed, and any exertion caused signs of dyspnoea. The carbuncle was still as Dr. Davidson had described it, with innumerable boils and pustules across the shoulders and down the back. There was an abscess on the left side of the chest; this had arisen painlessly as the patient was not aware of its presence. The tonsils and uvula were coated a gray tint with muco pus, and the patient's condition was extremely grave.

"He was undoubtedly suffering from septicemia. The urine was examined and now gave abundant evidence of the presence of sugar. A quantitative analysis was not made, but roughly two drops of urine were sufficient to reduce completely three quarters of an inch of Fehling's solution in a test-tube.

"Cultures from the open sores showed a mixed infection of staphylococcus pyogenes aureus and albus, with aureus predominating; cultures from the unopened boils and pustules were of pure aureus. The patient was treated with a vaccine of pure staphylococcus aureus prepared from the latter cultures. Inoculations were begun on June 11th with a dose of 250,000,000, increased to 500,000,000, afterwards to 750,000,000, and repeated every week. Subcutaneous inoculation caused abscess-formation at the site of injection, so that it became necessary to adopt the plan of injecting the inoculum deeply into the muscles to get away from skin contamination.

"Dr. Davidson kindly supplied me with the subsequent history. Between June 12th and 17th there was a severe entero-colitis, the patient passing as many as eighteen motions in 24 hours, and considerable quantities of blood-stained mucus and pus. As this condition improved cystitis developed, and a large amount of pus was present in the urine. A pretty severe attack of bronchitis came on later, and in all, nine abscesses in various parts of the trunk and lower extremities were opened.

"Under the influence of the staphylococcus inoculations the sugar in the urine gradually disappeared, and in the middle of August no trace of it was to be found. The last abscess, the ninth, formed in the lumbar region, and was opened on September 1st, after which the patient made

rapid progress and put on flesh. The original carbuncle had not yet healed. A sequestrum from the occipital bone was removed in October, after which the wound healed. For several weeks before the sequestrum was removed the patient was driving about looking after his usual work on the farm.

"During treatment two dozen inoculations were given, the dose latterly being increased to 1,000,000,000 of staphylococci. At no time during the illness was any attempt made to put the patient upon a carbohydrate free diet. In the acute stages every form of nourishment appropriate in any ordinary case to sustain the general strength was made use of.

"About a year later sugar reappeared in the urine of this patient and again vanished after a few inoculations of 250,000,000 of staphylococcus vaccine. No boils formed on this occasion."

Elsewhere I have recorded fully the following cases:

"An active business man, aged 50 years, was suffering from marked constitutional disturbance with local manifestation of infection. The digestive system had given trouble for years. His complexion was of the muddy appearance commonly associated with a bilious condition. There was a long history of constipation with all its attendant discomforts. While he was careful as regards diet there were periods of comparative comfort, but the digestive organs were always receiving medicinal attention in some form. A prominent characteristics was insomnia. The urine gave no indications beyond those usually found in severe digestive disturbances, until in a period of hard work and worry sugar made its appearance. Vision also became poor. A week later a boil developed on the lip, and he was sent to me. At once I started treatment with a vaccine of staphylococcus aureus, 250,000,000 being the initial dose. Four days later, taking the opsonic index, 1.47, to staphylococcus aureus as guide, I gave an injection of 500,000,000. The boil healed up very soon afterwards. The two doses more were administered after an interval of a week on each occasion. Sugar completely disappeared from the urine, refreshing sleep was enjoyed at night, and the general condition was greatly improved.

"Another case was that of a professional brother who had suffered for six months from an extensive furunculosis of the back of the neck and lower region of the scalp. Insomnia was painfully troublesome during the whole time, and sugar was present in the urine in considerable amount which dieting did not remove. Staphylococcus aureus was cultivated from the boils. The opsonic index to that organism was 7.7. A dose of 300,000,000 of an autogenous vaccine was administered with resulting marked local improvement and excellent general effect, for soon the insomnia was relieved. A dose of vaccine was given every week. Four weeks after beginning treatment the opsonic index was 2.7., and the furunculosis was at an end, but where the tissues had been indurated there was still a tendency to the formation of minute pustules, which were easily dealt with. In this case, as in others, chiefly I would direct attention to the digestive system. There had been no definite complaint regarding it, but I have no doubt that the insomnia was due to disturbance of the digestive organs by the invading organism and its toxins. Five or six days after the second inoculation there was a very sharp attack of diarrhoea lasting two days for which the patient could not account, and was inclined to attribute it to the effects of the vaccine. I consider that it was of the nature of a critical diarrhoea, and that the digestive organs had been suffering from toxic action, as evidenced by the presence of sugar, and a large amount of amorphous phosphates in the urine. After the fifth inoculation sugar was eliminated from the urine and a normal state of health had been established.

In neither of these cases has there been a return of boils of glycosuria."

PANCREATITIS.

I have had no experience with vaccines in the treatment of pancreatitis not complicated with glycosurea, nor have I seen any literature or reports of such cases treated by this method, but from the results in similar infections there is no doubt in my mind but that good results would follow their use. The same combined vaccine so successfully employed in infections of other abdominal viscera, containing the colon bacillus, the streptococcus, the pneumococ-

cus, and the staphylococcus would be indicated. Dosage and intervals between inoculations should be the same as in infections of other abdominal organs.

APPENDICITIS.

The present view among surgeons as to the best method of treating appendicitis is early and immediate operation, and aside from immunotherapy this position is undoubtedly correct. The appendix seems to be a favorite locality for infection, probably because of its peculiar construction and the fact that it is a rudimentary organ. It serves no known purpose and its removal is a comparatively simple, harmless surgical procedure under modern aseptic surgery. The danger from appendicitis is extension of the infection, and experience shows that there is less danger from extension of the infection in the early stages of acute appendicitis; before pus has formed, after the appendix is removed and when necessary drainage is established; but drainage does not invariably prevent extension of the infection. When immunization as a means of preventing extension of the infection is not employed, immediate operation is by all odds the safest procedure, but therapeutic immunization as a means of effectively preventing extension of infections is now well established, especially so when vaccines are employed early. Why not, then, employ this therapeutic measure in cases of appendicular infection as well as in other infections? There are many cases of appendicitis in which consent for an immediate operation cannot be procured, but where an immediate hypodermic injection of a vaccine would not be objected to. This would at least give some protection until the patient consents to an operation. In many cases a day's time will be required from the time the attending physician makes his first call until a competent surgeon is secured and arrangements made for the operation. If the attending physician gives a dose of vaccine at his first call the patient will have 24 hours' advantage

of the immunizing influence of the vaccine. As a rule it will be found that the more acute symptoms demanding immediate operation will have subsided within 24 hours after the first inoculation of the vaccine. At all events, the patient should then have another dose of vaccine. If operation is still considered necessary the immunizing influence of the vaccine will be sufficient to prevent post-operative extension of the infection, whereas, if the patient has made such progress that an operation is considered inadvisable, the prospect can be safely entertained that complete recovery will take place under further vaccine treatment. In cases where the infection has progressed to pus formation, when it is advisable to postpone operation until a more secure walling off of the abscess has taken place, immunization with vaccines is a most rational procedure. Furthermore, there are many cases of pain in the region of the appendix of a subacute or chronic character, where the diagnosis is too obscure to justify an immediate operation. In such cases therapeutic immunization with vaccines serves a good purpose. After a few inoculations at two to four-day intervals, the inflammation in the appendix or adjacent tissues will in all probability subside.

From my close association with many physicians who are using vaccines much information has been obtained as to the results from the use of them. The late Dr. W. C. Bunce, of Oberlin, Ohio, for example, in a conversation related the following experience: He was called to operate in a case of appendicitis in an old man. Upon examination he found extensive tenderness with inflammation involving the entire side from the liver to the appendix. From his age, extent of infection, and advanced toxic symptoms he considered an operation at that time too dangerous to warrant its being undertaken and instead advised a combined colon bacillus, streptococcus, pneumococcus, staphylococcus vaccine. The patient soon began to improve and after

a few more inoculations of the same vaccine completely recovered without an operation. He related other experiences with vaccines where operations, without therapeutic immunization, would have been necessary.

My experiences with the use of vaccines in the treatment of appendicitis convinces me that therapeutic immunization is of such great advantage that a dose of combined stock vaccine should be given at once in every case, whether the case is to have an immediate operation or not.

In referring to the advantages of vaccines in surgical cases, Madden, of Cairo, (Lancet, Aug. 7, 1915, p. 271) recommends the use of a stock colon vaccine before severe appendicitis operations and also before prostatectomy. Why not employ this method in the less severe cases as well?

Dr. E. N. Hawley, of Norwalk, Ohio, (Bacterial Therapist, April, 1910) reports the following interesting case:

"J. H., lad of 15. Purulent appendicitis. Chills, temperature 104.6 degrees F., vomiting, every indication of profound sepsis. On operation the abdomen was found full of pus, the appendix gangrenous and sloughed. The surgeon and two consulting physicians present at the operation pronounced the case as hopeless, and prognosed death in three or four days. I therefore administered 8 minims of vaccine containing streptococcus 100,000,000, pneumococcus 100,000,000, staphylococcus aureus, albus and citreus each 200,000,000, colon bacillus 200,000,000 per c.c. at once, before the patient recovered from the anesthetic. Eight minims of same vaccine were administered at intervals of three to five days thereafter. Good drainage and general good care was instituted throughout. The temperature was normal in three days, and remained nearly normal thereafter. The patient made a rapid and full recovery. The recovery was attributed by all to the beneficial influence of the vaccine."

In considering the treatment of appendicular infections some of my early experiences may be of interest. I have

practiced medicine long enough to have seen much of the evolution through which the treatment of this disease has passed. As a young practitioner 31 years ago, I took charge of a doctor's office for several months while he was on a vacation. Not long after he returned he contracted appendicitis; the leading physicians of Detroit had charge of his case, and I acted somewhat in the capacity of a nurse. The diagnosis was made early, but nothing was done except to give some drugs to obtain relief, and local applications made. In less than a week's time he died of peritonitis. This case left a profound impression on my mind. About a year later a close relative of mine, a woman aged 50, took sick with severe acute appendicitis. The former family physician was called in consultation and concurred in the diagnosis, but all he suggested was to keep the bowels open with castor oil. Not being satisfied with the progress that was being made I had Dr. McGraw, who was then the leading surgeon of Detroit, called to see the patient. He agreed with us in the diagnosis, but had no suggestion on treatment. As he was ready to leave the house I requested him to come back and at least make a vaginal examination. He did so and found a large abscess pressing downward. Her temperature then ranged between 103 and and 104 and the pulse from 120 to 140 and feeble in character. The abscess was drained per vagina on the next day, when a large quantity of foul-smelling pus was evacuated. Drainage tubes were inserted and the abscess cavity was flushed several times a day with antiseptic solution. Somewhat later the necrotic remnants of the appendix got stuck in the drainage tube and on removing the tube was withdrawn from the abscess cavity. After this healing progressed rapidly with an ultimate complete recovery.

A few years later I drained an appendicular abscess in a girl 8 years old by making an incision through the abdominal wall. Drainage tubes were inserted and inside of a month the wound healed, resulting in a complete recovery.

I did several more similar operations resulting in recovery, but my taste did not incline towards surgery, so as the operative procedure in treating appendicitis developed my cases were turned over to the care of surgeons. For a time all my surgical cases were turned over to the care of Dr. Fritz Maas, who had had an extensive surgical experience in Germany and made surgery an exclusive specialty. At that time he believed the safest procedure was to quiet the bowels with small doses of morphine, give no food, keep the patient at absolute rest in bed, and apply an ice bag over the appendix, allow sufficient time for an abscess to wall off, then operate by drainage. All my cases treated by this method under Dr. Maas' supervision recovered. Dr. Maas left Detroit, I think during the year 1899, and after that I had other surgeons look after my surgical cases, but when called on to treat cases of appendicitis I was naturally inclined to follow Dr. Maas' methods. From that time to the time when I began to use vaccines two patients died. One was a middle-aged man who was operated on by a leading, but old school surgeon. The abscess was readily reached, but to my judgment the incision was made entirely too large and in an attempt to explore the abscess, too much manipulation was entered into for the welfare of the patient. He died two days after the operation. The other case was a woman, aged 29; she was operated on three days after the onset of acute appendicitis by a leading surgeon. A small amount of pus was found around the appendix and the appendix contained a fecal accretion. No bacterial examination of the pus was made, but from the way the infection progressed after the operation I have good reason to believe that streptococci were present. The patient died four days later.

When I first began to use vaccines as immunizers in the treatment of appendicitis, a combined vaccine containing streptococci 30,000,000 and colon bacilli 40,000,000 per cubic centimeter was employed, but in my later cases a

more extensively mixed vaccine containing colon bacilli 200,000,000, streptococci 100,000,000, pneumococci 100,000,000, and staphylococci aureus, albus and citreus each 200,000,000 was employed, and I think to advantage. So far I have treated nineteen cases with the vaccine method and will briefly describe several of them:

Mr. D. was seen on Dec. 25, when he evidenced a well-marked appendicular inflammation. Temperature 101, pulse 120. I advised absolute rest in bed, an ice-bag, no food and gave a dose of streptococcus-colon bacillus vaccine. The next day pulse and temperature were about the same and by the 27th the temperature was 99 and pulse 120. Another dose of the same vaccine was given. The pain by this time was practically gone and patient feeling quite comfortable. On the evening of the 27th the temperature was normal and pulse 114.

Temperature remained normal and pulse came down to 84 by the 30th. The patient feeling comfortable with practically no pain. On the 31st the temperature was 99.5 and pulse 88. The same dose of vaccine was repeated and on the morning of Jan. 1 the temperature was 100 and pulse 100. In the evening the temperature was 99 and pulse 104. No material pain in region of the appendix but unmistakable signs of pus formation. The patient was taken to St. Mary's Hospital and a large appendicular abscess opened and properly drained. Bacterial examination of the pus showed colon bacilli and pneumococci. The presence of the pneumococcus to my mind explains why the inflammatory process was not aborted, the vaccine which was used having been streptococcus and colon bacillus. After this pneumococcus was added to the vaccine and inoculations repeated at from three to five-day intervals, eight more doses being used. He made a good recovery. The one feature of this case that impressed me very much was the practical absence of pain while this large abscess was forming.

Mrs. B. had had an attack of appendicitis about six years previously when I treated her with rest and an ice-bag and no food. At that time she made a good recovery. This last attack started with a severe pain during the night. She called in a physician from the neighborhood who gave her practically the same treatment as she had received for the previous attack. As she was not progressing favorably, she called me on the evening of the fifth day, stating that the other physician had insisted on the necessity of an operation, to which she would not consent. Upon examining her I felt that the other physician was right, there being an inflammatory mass about the size of a large orange, distinctly palpable in the region of the appendix. Her temperature was 100.4, pulse 99. I considered immunization before operation in such a case essential and accordingly gave her a dose of streptococcus-colon bacillus vaccine with the intention of advising an operation the next day. The ice-bag, no food and absolute rest in bed were continued. The following day her temperature was 99 and pulse 84 and she was feeling much better, the pain subsiding. On the 3rd the temperature was 100, pulse 96, but other conditions favorable. Another dose of the same vaccine was given. After that she continued to improve rapidly, she was given an inoculation on the 7th and the last on the 11th, when all the inflammatory condition had subsided. I inquired carefully about the character of the stool every day to ascertain if any pus had discharged but nothing of the kind was determined. I saw the lady recently and from all indications she is entirely well.

My son had had three slight attacks of appendicitis which were treated with rest in bed, ice and no food. During the spring of 1908 he had an attack which was more severe than the others. Temperature 101 with a distinct inflammatory bunch in the region of the appendix and the characteristic rigidity of the abdominal muscles. I was especially disappointed because this happened the week

before the A. M. A. meeting at Chicago which I was very anxious to attend. There was some improvement after the first inoculation and on the third day the vaccine was repeated. Twenty-four hours after the second injection the temperature became normal and the swelling began to subside. On the fifth day swelling and tenderness were all gone and everything looked so favorable that I attended the A. M. A. meeting. No further treatment was employed, the case resulting in a complete recovery. He is now 26 years of age and enjoys perfect health, not having had the slightest return of the trouble.

In one case the acute symptoms over the appendix subsided rapidly. I advised an operation and the appendix was removed, resulting in a complete recovery. All the other cases were treated with the same vaccine, making inoculations at from two to three-day intervals. They all made uninterrupted recoveries.

Dr. Southwick, of London, (New England Medical Gazette, January, 1912, p. 12) among other things refers to the following case: "Dr. Craig reports many interesting cases successfully treated by vaccines. Amongst others was a man 65 years old who entered the hospital at the end of a prolonged spree. He was on the verge of delirium tremens and had a very severe appendicitis. He was in such bad condition that it was considered hopeless to operate and the last rites of his church were administered. He was given a vaccine made from the interior of an appendix removed the day before from a very severe case of perforated appendix, the vaccine being ready for the patient in case he needed it. It consisted of a mixture of streptococci and colon bacilli. The patient made a remarkable recovery, was out of bed in a week and left the hospital four days later."

In making bacterial examinations following operations on those cases of appendicitis which have come under my care, pneumococci were found twice and streptococci once, while colon bacilli were found in all the cases. This includes

a few bacterial examinations made in other cases besides my own.

One of the most characteristic features following the vaccine treatment in appendicitis is the influence the vaccine has in relieving pain. As pointed out by Wright, this can be accounted for on the ground that when the immunizing powers are raised during an active infection the pain subsides.

Vaccines have also proved to be valuable agents to assist the healing process in suppurating wounds after appendix operations. In the treatment of this class of cases, Stone (Journal A. M. A., February, 1913) says:

"I have treated about twenty infections following appendicitis due to the colon bacillus, in which the wound area was soiled, either at the time of operation through the rupture of an adherent fragile appendix or previously. Each of the patients was discharged with the wound healed on an average three and one-half weeks after operation. The purulent discharge was in each case profuse, but was lessened after the second or third inoculation with a vaccine prepared from the patient's organisms and begun as soon as possible after the pus appeared. The dose varied from 30,000,000 to 50,000,000 every third day. The average stay of 25 cases with wound infection treated in the same institution and under similar conditions, but without vaccine, was approximately six weeks as contrasted with three and one-half weeks for the twenty patients treated with vaccine."

An interesting case of post-operative infection has come under my observation that was treated by Dr. A. T. Sherman, of this city. He makes the following report:

"Miss M. gave a history of having had attacks of pain in her abdomen at irregular intervals for about four years which would get better after medical treatment. In May, 1914, she had a rather severe attack which lasted about twelve hours. The doctor at that time pronounced it appendicitis and thought in time an operation would be necessary. She got better, but later on had a fall which brought

on another attack. Dr. Spitzly was called in consultation. She entered a hospital June 28 and was operated on by him for appendicitis June 29, 1914. She remained in the hospital for three weeks and was then taken home with the wound still open and a drainage tube in position. The wound was dressed daily by Dr. Spitzley or his assistant. About two weeks later better drainage was established by opening the wound and inserting drainage tubes. For about three weeks the doctor dressed the wound at her home and from that time to the middle of September the patient went daily to the doctor's office for a dressing. Then a second operation was considered necessary and performed. The patient remained at the hospital for three weeks. After returning home, again the doctor dressed the wound daily. Progress was slow and after a time abscesses began to develop in the side, discharging much pus. She kept growing worse steadily and when I first saw her on Dec. 26, 1914, she was most miserable indeed. She weighed about 95 pounds, although before the operation, had weighed 142. There was a large opening in her side discharging much foul pus. The previous attending physician dressed it every day with a gauze pack. No bacterial vaccines to control the infection had been employed. Her appetite and digestion were poor. She was thoroughly discouraged because she was steadily losing ground. There were three openings, one about an inch in diameter and two about a quarter-inch in size. Underneath there was an excavation six inches in one diameter and seven inches in the opposite direction. The cavity would comfortably retain a bunch of gauze as large as a man's fist. A large amount of bad-smelling pus, enough to completely saturate a pad two inches thick and twelve inches square twice daily, was discharged.

"I started vaccine treatment at once by giving 0.3 c.c. of a stock vaccine containing streptococcus 100,000,000, pneumococcus 100,000,000, staphylococcus aureus, albus, and citreus each 200,000,000, and colon bacillus 200,000,000 per c.c. Meantime cultures were taken for making a bacterial examination. The wound was dressed by the usual method, cleansing, gauze, and drainage each day. Bacterial examination of cultures showed colon bacillus, streptococcus, and staphylococcus. The mixed stock vaccine was continued by inoculations at five-day intervals, while

gradually increasing the dose. Improvement was soon noticed by a marked decrease in the amount of pus, and the patient soon began to eat better. No more abscesses developed after the first inoculation. The wound granulated and healed rapidly. She was able to call at my office for treatments at the end of February and by April 11, 1915, resumed her former occupation. Since then she has married and feels entirely well."

COLITIS.

Diarrhoeas due to chronic infections of the colon, while not common, are of sufficient occurrence to deserve consideration. Bacterial examinations of the stools do not offer any conclusive evidence as to what infecting organisms cause the inflammations of the colon, because such a large variety of germs are present at all times in the feces under normal conditions. In our laboratory work we have made bacterial examinations of clumps of mucous, but nothing distinctive in character was found. Streptococci, colon bacilli, pneumococci and staphylococci were found. By associating the fact that one or more of these organisms are responsible for gastric infections and that the same organisms are the etiologic factor in hepatic and gallbladder disturbances, it is reasonable to assume that chronic catarrhal infections of the colon may also be due to the same cause. Many of these cases are also affected with chronic mouth infections, which would also indicate that the bowel infection is due to the same organisms.

Allen ("Vaccine Therapy," fourth edition, p. 227) refers to work done by Butler Harris, Eyre, Wilcox, Matthews, and B. Dawson, in which favorable reports have been made from the use of autogenous vaccines. He reviews this work in part as follows:

"Thus Butler Harris employs doses of 10,000,000 B. coli at weekly intervals, and states that 'the patients soon put on weight, improve in general health, and pass no more blood or mucous. Several of them are now well for over two years; two others, however, require occasional inocula-

tion. The patients know when they are losing ground, and present themselves for treatment. I venture to think that in severe cases of colitis, appendicostomy, followed by vaccine treatment, would be the most desirable course to adopt. Certainly inoculation gives better results than washing out the bowel!

"Hale White describes the case of a young man aged 17, who had suffered from ulcerative colitis for many years, and in whom every form of treatment had been tried but opening the appendix and vaccine treatment. A vaccine of his B. coli was tried, with the result that the temperature immediately began to fall, the motions became more normal, the passage of blood ceased, and he is now well, of normal weight, and earning his living. He finds that the results are not always so striking as this, and that progress is often very tedious, and that very often several forms of treatment have to be conducted simultaneously.

"Willcox has found autogenous vaccines of decided help in cases which do not respond to ordinary medical means, and holds that they should always be tried before the abdomen is opened, except in very acute cases.

"Dawson describes three cases in which at least considerable improvement was brought about. While convinced of the good results, he feels that bacterial infection is not the only cause of colitis, but that it is rather a direct causal factor of varying import, in some cases more dominating, and in other cases less dominating."

Dr. W. J. Buck (The Bacterial Therapist, November, 1914) reports two interesting cases of chronic diarrhoea treated with a combined colon bacillus, streptococcus, pneumococcus, staphylococcus stock vaccine with good results. One case was that of a lady 57 years old. Loose movements of the bowels would start at 4 o'clock in the morning and continue until noon. The stools were very thin, accompanied with gas and almost uncontrollable. She had suffered with this diarrhoea for 25 years, and on account of this trouble did not trust herself to leave home. She also suffered with rheumatic pains in her knees. After three months' treatment with this combined vaccine, receiving

in all twelve inoculations, she was cured. The other case was a man aged 67. He had chronic diarrhoea for 20 years. Being well-to-do he had consulted many physicians in this country and abroad. His stools were also watery, but not copious and aggravated as in that of the woman. The same stock vaccine was employed with equally good results.

These cases at least indicate that inflammatory conditions of the colon are due to the same pyogenic micro-organisms that are responsible for infections in other parts of the digestive tract, and justify the use of a combined streptococcus, colon bacillus, pneumococcus, staphylococcus vaccine. I have had some experience with this combined vaccine in the treatment of protracted diarrhoea in infants and children with good results. I am satisfied that an irritated condition of the bowel from any source will favor pyogenic germ development on the mucous surface of the bowel and that immuno-therapy with vaccines will offer material aid in the treatment of these cases.

Rectal Fistula.

In cases of rectal fistula the question of a possible tubercle infection should always be carefully investigated and when present specific antitubercle treatment instituted.

Aside from tubercle infections the infecting organisms responsible for rectal abscesses with resulting fistulae are the usual pus-producing organisms: staphylococci, streptococci, and colon bacilli. A mixed vaccine containing these organisms is indicated.

Early vaccine treatment in these cases is important. If vaccines are employed during the early inflammatory stage, antecedent to pus formation, the course of the infection can be aborted and pus formation avoided. If the case is seen later, however, vaccines will still be beneficial in that the abscess will be less extensive and less painful and will heal so rapidly after drainage is established that a fistulous opening will, with rare exceptions, be avoided. The vaccine

should be given in the dosage and at the intervals employed in other moderately extensive acute infections.

In cases of a fistula of long standing it is always well to give a combined vaccine of the staphylococcus, streptococcus, and colon bacillus at four or five-day intervals for a few weeks as a trial. I have seen such cases permanently cured by this method. If no progress is made surgical measures should be employed. The vaccine treatment, however, will not have been in vain. The immunity thus established will be of great benefit in hastening repair by preventing post-operative extension of the infections. In this connection it may be said that this same principle applies to operations on the rectum for other disease conditions. A sterile field is practically impossible in operations on the rectum and for that reason prophylactic inoculations of a suitable mixed vaccine should always be employed before operating.

PRURITUS ANI.

Dr. Dwight Murray reported some original work as to the etiology of puritus ani in the Dec. 9, 1911, number of the Journal A. M. A. He finds that the ailment is due to a streptococcus infection of the skin around the anus. He contends that the organism is a specific type of streptococcus of the fecalis variety. Since then he has made several reports confirming his original contention as to the infectious character of the disease.

He isolates the organism and prepares autogenous vaccines in the treatment of his cases. The results have been uniformly good. The dose is sometimes worked up to 2,000,000,000 organisms. He finds that in some cases it is difficult to grow the germ and attributes this to the comparative non-virulence of the streptococcus causing the infection.

I have recently treated one case with a polyvalent stock streptococcus vaccine combined with a colon bacillus, pneumococcus, and staphylococcus. The case was of one year's standing. Itching subsided after the third inoculation and from present appearance a permanent cure will be effected.

CHAPTER XIII.

SKIN INFECTIONS.

General Consideration.

In no class of diseases has the use of vaccines proved more thoroughly effective than in the various dermatoses. Some of the earliest work with bacterins has been done in this specialty. This has been undoubtedly due to the fact that infections of the skin are so common, the infecting organism so easily identified, and the results of the treatment so readily observed.

Since so many disease conditions of the skin are caused by germs, it is quite natural that antiseptics of various kinds are extensively used in the treatment of these ailments. The value of local antiseptics is largely dependent upon whether the infection is superficial or down in the follicle.

Obviously surface infections are more readily cared for by this method than deep-seated ones, but in treating skin diseases the destruction of the infecting organism is not the entire problem. Staphylococcus and other infecting organisms are normally found as saprophytes on the skin and only become pathogenic when conditions arise which make a deeper invasion of the tissue possible. The most important of these conditions is a lowered resistance to the infecting organism.

Local treatment may effect a cure, but from the want of sufficient immunity the condition often returns. By using vaccines, however, the treatment is directed towards raising the immunizing faculty, thus establishing a more prompt and more permanent recovery.

The staphylococcus being present on the normal skin, it naturally follows that this organism is either the primary cause or a complicating factor in skin infections. Strep-

tococci are also common in both acute and chronic inflammations of the skin. The colon bacillus is liable to become a factor in chronic ulcers and sometimes produces abscesses. The bacillus pyocyaneus, the typhoid bacillus and other organisms, may also cause abscesses. In acne the acne bacillus is the principal offender. Lupus will be considered under tubercle infections.

ERYSIPELAS.

Of the various skin infections met with by the general practitioner, erysipelas is the most serious. That the streptococcus, usually of the long chain variety, is the cause of the infection, is now well established. Clinical symptoms are sufficiently characteristic to enable an early diagnosis; in fact a clinical diagnosis can, as a rule, be made in less time than a culture could be incubated and examined. From an extensive experience in taking cultures from cases of erysipelas, I find that the streptococcus is not as easily found as might be expected. I have never isolated streptococci from cultures procured from blebs; staphylococci always being found in abundance. Cultures from pus, where an abscess developed in the deeper tissues, always showed streptococci in great numbers. Where no pus has developed I find the best way to procure cultures is to make small cuts through the skin and then press out blood and serum from the deeper structures. In this way about one out of three cultures will yield streptococci.

As in other acute infections, early treatment is important to procure the best results. The theoretical contention that vaccines are not applicable in severe acute infections largely accounts for the reluctance displayed by many physicians to apply vaccines in erysipelas. Some of my early experiences in the use of vaccines were in cases of erysipelas and from the results obtained there was no question in my mind concerning their therapeutic value, regardless of theoretical considerations.

Existing information as to the best methods of employing vaccines in erysipelas has been gradually collected. Frequent communications from physicians relating their experiences with vaccines in erysipelas have been a valuable addition to my own experiences. For some time we were inclined to use small doses and not repeat inoculations unless clinical symptoms indicated a revival of the infection, by rise of temperature, increased pulse rate, increased tenderness and extensions of the inflamed area. This cautiousness was based on the theoretical conception that in toxic infections small doses and guardedness in repeating inoculations are necessary to avoid a dangerous negative phase. Gradually, however, it was found that negative reactions were not encountered with comparatively large doses and that inoculations at short intervals were of distinct advantage. This is in entire accord with experience in the treatment of other severe acute infections.

A stock vaccine prepared from four or five strains, isolated from erysipelas cases, should be employed. Because of the fact that staphylococci are found in such great abundance in the inflamed area it occurred to me that this organism is a complicating factor of some importance in this disease and accordingly I combined staphylococci with the streptococcus erysipelatis in the preparation of a vaccine. The dose should be 50,000,000 of the streptococcus erysipelatis and 200,000,000 staphylococcus, and treatment started early. The vaccine inoculation should be repeated the next day, and thereafter at two or three-day intervals. If the vaccine is given before the infection has had time for spreading extensively—during the first and not later than the second day—the course of the disease will be aborted, a speedy recovery occurring. Such striking results are not secured when the vaccines are employed later in the course of the disease, but even in advanced cases marked beneficial results are obtained, unless the case is already moribund. In extremely bad cases it is

advisable to give two doses of vaccine the first day, and then inject it at daily intervals for two or more days. A reduction of temperature with subsidence of toxic symptoms such as nervousness and delirium should ensue within one or two days. The inflamed area will not be so pronounced and the swollen margin not so elevated. Where pus formation has taken place, proper drainage is necessary. After the more acute symtoms have subsided, vaccine treatment should be continued at four to six-day intervals for several more inoculations.

Spontaneous recovery from an attack of erysipelas often leaves the person more susceptible to subsequent attacks, showing that the live virulent organisms do not influence tissue cells for permanent immunization, but on the contrary have a tendency to break down the immunizing mechanism. If vaccine treatment is continued however, for a month or two, making inoculations at weekly or two week intervals, an immunity can be built up which will be fairly permanent.

From reports of cases treated in hospitals it appears that the results have not been as good as in cases treated in private practice. This is accounted for by the fact that hospital cases are usually far advanced before they are taken there, and consequently treatment is started too late to obtain the best results. The most favorable report that I have seen from hospital practice is by Ross and Johnson (Journal A. M. A., 1910, p. 966). They treated with vaccines 50 cases admitted to the Toronto General Hospital during 1908, and compared the results with 19 cases treated during 1907 without vaccines. Stock vaccines were employed. Of the 50 cases admitted, 18 were very severe, 20 were severe, and 12 mild. The most pronounced effect of the vaccine treatment was a marked and rapid relief from toxic symptoms with a relief from nervousness and delirium. Even very severe cases looked and felt better, especially after the second inoculation, given the second day. The

inflammation usually extended a little but was not so angry red in appearance, the skin was less swollen, much less tender, and painful, and the extending margin practically level and fading into the healthy skin. In severe cases 10,000,000 streptococci and in the less severe 20,000,000 were given. The dose was repeated the second day and in very severe cases the repeated dose was often reduced to 5,000,000. There was but one death, and this case was moribund when admitted to the hospital. The average length of illness of cases treated without vaccines was 25 days while in those treated with vaccine the average was 12.8 days.

This is certainly a good showing. From my experience, however, I am confident that even better results would have been obtained if larger doses of vaccine had been employed.

Manard Smith considers the vaccine treatment of erysipelas the most reliable means at our disposal. He advises daily inoculations of vaccines for the first few days.

Dr. E. Mather Sill, reports ten cases of erysipelas treated with vaccines, in infants ranging in ages of 17, 12, 11, 8, 5¾, 5 months and one 8 days old. Of the ten cases treated one died. Streptococcus vaccine was given in doses ranging from 50,000,000 to 120,000,000, and in some cases staphylococcus and colon bacillus was added. When we consider the usual high rate of mortality from erysipelas in infants this is a remarkable showing. It will be noticed that large doses were employed.

Dr. Arthur Schnell, of Detroit, had an interesting case, in which he consulted me, where the infant contracted erysipelas six days after the confinement:

The mother gave a history of having had facial erysipelas three times, the last time two months previously. On the day of confinement there was some inflammatory redness on one cheek but this subsided. The labor was such that instrumental delivery was necessary. On the second

day after the confinement a temperature of 105 developed with the pulse at 130. With the idea that there might be some retained placenta the patient was taken to St. Mary's Hospital and curetted, but nothing was found. A dose of stock streptococcus and staphylococcus vaccine was given. The next day no material improvement was observed. I was then consulted, and basing my judgment on the history of the case advised a stock streptococcus erysipelatis vaccine. The day following the temperature was 100 with other conditions improving proportionately, and two days later it was down to 99. Three doses of streptococcus erysipelatis vaccine were given at two-day intervals, when the temperature became normal and the patient felt quite well. A week later, however, the temperature again rose to 105. The same vaccine was once more resorted to with very gratifying results. In two days the temperature was down to 100, and under three more inoculations at two-day intervals the case went on to complete recovery. This case was unusually severe from the start, and the relapse taking place when the vaccine was discontinued with prompt recovery after resuming it, conclusively shows its value.

About seven months after the confinement she developed an acute attack of erysipelas on the leg, which cleared up after three inoculations of streptococcus vaccine.

When it was 6 days old the baby also contracted erysipelas. It was treated with the same vaccine and after three inoculations at two-day intervals made a good recovery.

IMPETIGO.

This is one of those disagreeable skin diseases which does not do well under drug or local treatment. Staphylococci and streptococci are found to be the infecting organisms. A combined vaccine containing these organisms should be employed. Treatment is started by giving streptococcus 30,000,000 and staphylococcus aureus and albus each 200,000,000, and repeating inoculations at three or

four-day intervals, gradually increasing the dose to streptococcus 60,000,000 and staphylococcus 500,00,000. Improvement will be observed soon after using the vaccine. Cleanliness, removing scabs by applying moist pack and boric acid solution, should be employed to facilitate the healing process.

VARICOSE ULCERS.

In the treatment of varicose ulcers, we have two essential conditions to deal with; congestion due to imparied circulation, and infection. Both of these factors must be dealt with to obtain the desired results. To relieve the congestion, rest in bed with the leg elevated answers the best purpose; but many such patients are working people who cannot afford idleness. A suitable bandage applied on rising in the morning and worn all day will do much towards relieving the congestion and keeping the swelling down, but relapses are so common that many cases are abandoned as hopeless. The persistence of this ulcerated condition with indolent surfaces, sharply defined borders, and absence of healthy granulation is undoubtedly due to infection.

Staphylococci, streptococci, pneumococci, and colon bacilli are the most common markedly pathogenic organisms found. The bacillus pyocyaneus, bacillus proteus, the pseudo-diphtheria bacillus, or other organisms are also sometimes present.

A combined stock vaccine containing staphylococci, streptococci, pneumococci, and colon bacilli is usually employed and inoculations made at five to seven-day intervals. Healthy granulations will develop soon after instituting vaccine therapy, and if this is combined with the other measures usually employed the healing process will progress rapidly.

Dr. Huegli (Bacterial Therapist, April, 1914) gives an

account of six cases which cleared up in three weeks or less after using mixed vaccines and local treatment.

Dr. Joseph V. Becelaere, of Detroit, has used mixed stock vaccines regularly in his work for some years and finds them of great advantage, in conjunction with other measures, in procuring healthy granulation, and thus stimulating the healing process.

CARBUNCLES AND BOILS

The staphylococcus is almost invariably responsible for the development of boils and carbuncles. Generally it is the staphylococcus aureus, but in the less severe types the albus is sometimes responsible. Both the staphylococcus aureus and albus are also found in some cases.

The low resistance of the individual to the staphylococcus is evident from the tissue destruction and inflammatory infiltration that usually takes place before it runs its course. The tendency to recurrences also indicates that a general immunizing resistance is not developed spontaneously during recovery from a boil.

An early diagnosis is readily made; the intense localized tenderness with the throbbing pain are very characteristic. Early treatment is very important. If the vaccine is given before a necrotic center has developed the infection can be aborted. I have seen this done repeatedly. When the infection has extended to pus formation with some tissue destruction the inflammation around the necrotic center will become less angry and recede, leaving a small inflamed area in close proximity to the center of infection. The boil can then be readily opened and drainage will be free because the surrounding tissue is not so intensely swollen that the opening is encroached upon. In the still farther advanced cases, where extensive inflammatory infiltration exists with several openings good results may be obtained in that the infiltration will subside sooner and a more rapid recovery take place.

One of the most characteristic influences of the vaccine when used in the treatment of boils is relief from pain. Some relief is often felt twelve to eighteen hours after the first inoculation, and as a rule, the patient is quite comfortable in twenty-four to thirty-six hours.

Treatment should be started by giving 200,000,000 each of a polyvalent stock staphylococcus aureus and albus vaccine. In advanced cases the same dose should be repeated the next day. After the extremely acute symptoms have subsided, inoculations should be made at from two to four-day intervals, with increasing doses. The final healing proceeds rapidly, but to secure permanent results it is advisable to continue treatment by giving a few more inoculations at weekly intervals. To build up a lasting immunity these cases often require inoculation at three or four-months' intervals over a period of several years.

Ross cites a case: (Journal A. M. A., Oct. 12, 1907, p. 1246.) "The patient was a laborer of 45 who had a carbuncle on his back as large as a baby's fist. Inoculation with 300,000,000 staphylococci removed all pain and tenderness in forty-eight hours, the central slough came away in eight days and almost all of the inflammation mass was dissipated a week later."

ABSCESS

Abscesses often develop after some acute infectious disease, like typhoid, scarlet fever, or some remote infection. Abscesses as a result of lymphatic involvements from throat infections in infants and children are not uncommon. The bacteriology in such abscesses usually corresponds to the organism causing the original infection, and naturally a corresponding vaccine should be employed.

Abscesses that develope from lymphatic involvements as a result of throat and mouth infections in infants and children, deserve special consideration. In these cases a hard

indurated inflamed area, develop from the lymphatic glands of the neck which break down with extensive abscess formation when left to run their course. By employing a combined streptococcus, pneumococcus, staphylococcus vaccine early, before destructive processes have had time to develop, enough immunization will take place to avoid abscess formation. I have succeeded in doing this on several occasions. It will also be found that if vaccines are employed later, after the infection has developed to a point where abscess formation can no longer be avoided, the inflammatory infiltration around the infected center will become less even before the abscess is drained. The little one also shows indications of less suffering by not being so restless. This same condition holds good when vaccines are employed in cases of scarlet fever.

FURUNCULOSIS.

Furunculosis is so uniformily due to staphylococcus infection that a bacterial examination of the pus is not as a rule necessary. The staphylococcus aureus is most frequently found but the albus variety is also frequently present. A combined polyvalent staphylococcus aureus and albus stock vaccine serves every purpose.

The use of staphylococcus vaccine in the treatment of furunculosis serves as a classical illustration, showing that live virulent organisms in an active infection are not as efficient in stimulating tissue cells for antibody production as killed germ inoculations. Furuncles have a distinct tendency to relapse and become chronic; new furuncles continually appearing while the old ones are healing and this may continue over periods of months or years. Every one of these furuncles will cause more local and constitutional disturbance than a staphylococcus vaccine inoculation and yet one dose of vaccine will stimulate more antibody production, as shown by the clinical results than developed from the combined influence of all the furuncles

extending over a period of months or years. A case reported by Dr. A. P. Biddle (Bacterial Therapist, April, 1913) which I saw when he was taken to St. Mary's Hospital for treatment, offers an illustration:

J. S., age 29 years, admitted to the hospital suffering with extensive skin lesions which involved both lower limbs. The lesions were circumscribed inflammatory areas—many of which had already reached stage of suppuration.

Patient had suffered with this condition for the past six years and during this time had continually been under treatment with no results. Upon examination it was found to be a pure staphylococcic infection and diagnosed as furunculosis. Treatment: Sherman's staphylococcus vaccine 200,000,000 was injected; no marked change in three days, second injection given. The following day the lesions began showing signs of disappearing; aforesaid dose was repeated every third day until five doses were given. Patient left the hospital at the end of thirteen days with not a sign of a furuncle.

Allen (Vaccine Therapy, Third Edition, p. 92) sums up his own experience and that of others as follows: "The results recorded by many observers in boils and carbuncles, of which the greater proportion are due to aureus, have been uniformly good. Thus, Whitfield says: 'In all the cases of furunculosis which I have treated I have obtained complete, and up to the present, durable success.' Western: 'Nine cases of furunculosis were treated with aureus vaccine, in every instance with completely satisfactory results. All the cases of carbuncle were ones which, in spite of incision, fomentations, and local antiseptics, showed no adequate attempt to repair or healing, yet all made rapid recovery.' Hartwell and Lee draw the following conclusions from their results in 100 cases of 'aureus' infections: 'Treatment with vaccines is the most effectual treatment for boils and carbuncles. There is marked diminution in

the pain and tenderness. After twenty-four hours there is a profuse discharge, which continues till the focus clears up. With boils about the face, the especial value of the treatment is the prevention of scarring. Although the vaccine treatment does not prevent recurrence, cases of chronic furunculosis can be absolutely controlled by occasional inoculation.' The initial dose is from 100,000,000 to 250,000,000."

Dr. W. H. Watters (New England Medical Gazette, Jan. 1912, p. 14) says: "Propably of all diseased states treated by this new method, no one has given so uniformly successful results as has furunculosis, not only in abating the severity of individual abscesses, but in eradicating the tendencies toward remissions or recurrences. So true is this that I do not look for criticism from any source from the sincerely believed statement that vaccine should be given preference over all other therapeutic measures in every case of furunculosis, using various adjuvants, surgical or otherwise, only as the individual needs seem to require."

Gilchrist (Congress of American Physicians and Surgeons, 1910, p. 165) says: "The staphylococcus aureus vaccine was used at first on furunculosis with beneficial and curative results to prevent relapses, but if a boil had formed, and especially with a necrotic plug, this had to be treated locally as well. I found later that the staphylococcus albus vaccine acted just as well as the staphylococcus aureus vaccine for furunculosis. About twelve patients were treated with the former vaccine and all were cured with the aid of this mode of treatment. Some cases had received local treatment and kept relapsing, and it was noticed that the use of vaccine stopped the relapses."

I usually start treatment with 200,000,000 each of staphylococcus aureus and albus making inoculations at three to five-day intervals. After the second or third inocu-

lation the dose should be increased to 300,000,000 or 400,000,000.

It is necessary to work the dose up to 1,000,000,000 or 2,000,000,000 in some cases, before a permanent cure is effected, and in these obstinate cases it is good practice to give a short course of treatment twice a year for several years to guard against a recurrance.

ACNE.

Acne divides itself into two classes of cases. The pustular form in which the pustules are superficial, and the nodular form, in which comedones predominate.

In the pustular variety the staphylococcus albus is the chief infecting organism and in this class of cases good results are being obtained with staphylococcus vaccine. In treating these cases, local treatment of the skin should not be neglected. Where deep-seated pustules exist they should be lanced with a cataract knife and the pus evacuated and local antiseptics should also be employed to take care of the surface infections. Either the staphylococcus albus or a combination of staphylococcus aureus and albus may be used. The dose varies from 200,000,000 to 600,000,000 and inoculations may be made at from three to seven-day intervals. In most cases it is advisable to start with the smaller dose and work up to the larger.

In acne vulgaris of the nodular variety where the skin is filled with comedones, the acne bacillus is regarded as the chief pathogenic factor. Gilchrist (Congress of American Physicians and Surgeons, 1910, pp. 172, 175, 176) was the first to describe this organism and to give a better understanding of this I will quote extensively from his report: "In 1899 I found a bacillus, which I named Bacillus Acne, in acne in 96 pustules and nodular lesions from 55 patients and obtained eleven pure cultures of bacillus acne on glycerine agar. I proved that this bacillus was pathogenic in animals from which pure cultures of the organisms were

again obtained. During the period of that work, there was no difficulty in growing the bacilli on ordinary glycerine agar. In 1903 I confirmed my previous work by finding the bacillus acne present in 240 smears from 86 patients and pure cultures of bacillus acne were obtained from 62 lesions. Sections showed that nodular acne was a giant cell granuloma and clumps of bacilli were found in the section stained by Gram's stain. I also found that the sera of patients suffering from severe acne caused clumping or agglutination of the bacillus acnes, even when diluted 1-100 and 1-200, which caused me to think that the anemia, coated tongue and constipation probably were the result of acne and not predisposing causes of acne. Others have confirmed my observation, notably Engman of St. Louis, Fleming and Western of England, and others. Fleming of London, as well as myself, has noticed that when too much vaccine is used a 'flaring up' of acne nodules appears after a few days and pure cultures of bacillus acnes can be obtained from them. This is a further proof that the bacillus acnes is the cause of acne, being similar in principle to the tuberculin test. . . .

"As the result of my experience with the treatment of acne during the last three years, I should say that vaccine therapy is of undoubted value, and in many cases curative. Of the vaccines to be used the staphylococcus albus vaccine is very helpful in cases of superficial pustular type—that is, when the staphylococcus albus as a secondary invader predominates—but where the nodular variety is present, then the bacillus acnes vaccine is the proper remedy to use. One would be apt to conclude from this, then, that mixed vaccines would be the ideal treatment. Even with vaccine therapy some cases are apt to relapse, because I think the patient's general condition is apt to relapse and so present favorable soil for the organism to proliferate again and cause new lesions. The bacillus acne is normally present in the skin and waits for an opportunity to grow, and since some patients are far more susceptible than others, the relapses more often occur in those cases. I recommend the

dose to be given at first to be about three to five millions, then gradually increase each week, but if new nodules appear three days after the injection then too much vaccine is being given. A great many of my patients were rid of their acne after seven to ten injections.

"In patients who have no acne lesion, but who in young adult life have, over nose and cheeks, numerous patulous openings out of which can be expressed thorny plugs or comedones, this bacillus acnes vaccine has been used with some success, but all the comedones must be expressed first. The vaccine has no effect whatever on comedones. One patient, a physician, has improved so much that he considers himself cured. Bacillus acne vaccines had also a beneficial effect on the oily seborrhoea which accompanied the presence of acne, but its results were not as good as the application of X-Ray."

The acne bacillus is a difficult organism to isolate and grow and for this reason autogenous vaccines are not practical, nor do they appear to be of any advantage where they have been employed. Autogenous vaccines are often prepared from the staphylococcus and stock acne suspension added.

In the application of acne vaccine there is a difference of opinion as to whether the acne and staphylococcus should be combined or the acne suspension and staphylococcus suspension used separately. Dr. Philip F. Shaffner, instructor in the University of Illinois (Bacterial Therapist, October, 1915), advises the use of acne bacillus vaccine alone in cases of comedones where no pustules are present, and those complicated with pustules staphylococcus albus is used separately. He contends that by not mixing the two organisms in the vaccine the dosage can be more accurately regulated. Dr. C. Augustus Simpson, of George Washington University (The Virginia Medical Semi-Monthly, August 8, 1913), also recommends acne vaccine uncombined with staphylococcus where comedones and no pustules are present. Where a pustular condition exists, he uses a

staphylococcus vaccine separately in conjunction with the acne vaccine.

Many physicians preferably employ the acne bacillus combined with the staphylococcus albus in the vaccine, and I can see no good reason why the two organisms may not be advantageously used together in a vaccine. Theoretically there can be no objection to having a high degree of immunity to the staphylococcus in the presence of an acne infection and experience does not indicate that there is any disadvantage in employing an acne vaccine which also contains a staphylococcus.

There is some difference of opinion on dosage in the use of acne vaccine; some recommend large doses, but most observers cling to the small dose. My observations lead me to favor the smaller doses, because with this organism, a negative phase will develop if too large doses are employed. The initial dose of acne bacillus vaccine should be from 3,000,000 to 5,000,000, and reactions should be carefully observed. By reactions it is the focal reactions, reactions in the infected area, that are meant. If three to six or more new pustules develop within 24 or 48 hours, the dose has been too large. The next dose should not be repeated until the reaction has entirely subsided and conditions appear to be at their best, which may be anywhere from the fourth to the tenth day after the inoculation, but usually about the fifth or sixth day. If the previous dose appears to have been too large the next dose should not be increased. Where no material reactions follow an inoculation, as shown by new pustule development, the dose may be increased by one to three million for the next inoculation. By carefully observing reactions and continuing the treatment over a long period of time the dose may be worked up to 40,000,000 or 60,000,000, but such large doses are not often used to advantage. The staphylococcus albus vaccine is used in about the same dosage employed in treating

furunculosis, starting with 200,000,000 and working up to 1,000,000,000 organisms.

The results from the use of vaccines in acne are very good, often brilliant, in about 50 per cent of the cases and in the rest of the cases the results depend largely on the faithfulness with which other treatments are followed up in conjunction with the vaccine and the persistance in treatment and care that is taken in gauging doses and repeating inoculations.

There is no disease that is "more treated" by the patient and more neglected by physicians than acne. In this regard Dr. C. Augustus Simpson well says:

"It is unfortunately true that a great many medical men treat this common affection with little short of contempt. There can be no real excuse for neglecting it. True, the treatment is tedious, relapsing, and relatively unprofitable to the physician, but the results, considering the relief of such a disfiguring affection and the conservation of human happiness, should appeal to every medical man even if he is occupied in other and apparently more important operations. It is a mistake to think these girls and boys endure their defacement with philosophical resignation. The disposition is often affected to a great extent, some girls becoming wretched, dejected and sensitive, oftentimes leading lives of seclusion to the great annoyance of the other members of the family and their friends.

"The advice they usually receive that the condition will clear up in time is true, but from that long drawn out process the girl emerges with a pitted and scarred face which she carries through the days when attractiveness and beauty are the attributes she most earnestly desires."

The local care of the lesions is of utmost importance in obtaining the desired results, and care should be taken that this treatment is applied at the proper time. Soon after giving the vaccine the patient passes into the negative phase. This lasts about two days and during this time no

local treatment should be employed because any kind of irritation during this time has a tendency to aggravate matters. Two days after an inoculation the patient passes into the positive phase and for about two days careful attention should be given to local measures. The patient is directed to then apply hot moist applications, press out comedones and manipulate the skin to increase the blood supply to the infected foci. I have found that gasoline, carefully applied with absorbant cotton and never near a fire, naturally aids in softening the crusted ends of the comedones, when they can readily be pressed out. Pustules that make their appearance should be opened and where possible the attending physician should do this. These pustules are often deep-seated and should be opened with a cataract knife. The pustules should never be cauterized with carbolic acid or other chemicals that have a destructive influence on the tissues because such treatment will cause unsightly scars and pits. If four or five new lesions appear within one or two days after an inoculation, the preceding dose of acne vaccine has been too large. The next dose should then be about the same or slightly smaller than the preceding one. It is better not to manipulate the skin or give local treatments for a day or two prior to the next inoculation. Usually in five or six days the skin condition is at its best, and then is the opportune time to give the next dose. Sometimes this opportune time will be on the seventh or eighth day. By directing the patient's attention to this matter the selecting of the opportune time to get another inoculation will soon be learned.

Persistence both in the use of vaccines and local care of the skin are the essentials in procuring ultimate success. I have had cases that appeared hopeless, relapsing after getting better, but by continuing the treatment for six months or a year ultimately get well. Some cases are stubborn and remain the same. Sometimes I have found that by changing to a mixed vaccine containing streptococcus,

pneumococcus, staphylococcus, aureus, albus, and citreus and colon bacillus, improvement will soon follow. I have not been able to explain to my satisfaction why this should be so. This combined vaccine has, from my experience, an unquestionable good influence on the digestive organs. Digestive disturbances have been recognized as an important factor in acne. It is possible that the combined immunizing and tonic influence of this vaccine accounts for the results obtained. Over eating and other indiscretions in diet are to be avoided.

Eczema and Psoriasis.

The advantages of this method are very beautifully illustrated in certain cases of staphylococcus infections such as eczema and folliculitis of the moist variety. Here the skin is literally bathed with blood serum oozing from the follicles, but being of low immunizing power the germs continue to grow without apparent hindrance. In many of these cases local antiseptics are of little avail, while staphylococcus vaccines give prompt relief.

The following case is a good illustration: Mrs. R., age 40, a short, corpulent woman, was suffering with moist eczema. The trouble started at the vulva with intense itching and continued to spread until it involved the legs to both knees and up the trunk to the belt-line. She had been under the care of several good physicians for six months but informed me that none had benefited her.

The woman was of very cleanly habits and felt much mortified about her condition. There was so much serum oozing from the skin that her clothing was always soiled. The itching and burning was such that she could not rest at night. From her statements I ascertained approximately what local treatments had been employed and from the results obtained felt that to continue local treatment would be of no avail. Staphylococcus aureus and albus mixed stock vaccine—200,000,000 of each organism—was re-

sorted to and all local treatment discontinued. In two days she felt much better, the itching and burning diminishing. By the sixth day, when the dose of vaccine was repeated, the skin had dried up and was healing. I requested her to return for a third inoculation in a week, but she felt so well she did not return for several weeks, when she came to pay her bill. By that time the skin had entirely cleared up and about two years later when I saw her again none of the trouble had reappeared. In this case evidently the immunizing powers against the staphylococcus were not adequate until they were raised by the stimulating influence of the vaccine, and when once actively established, became permanent.

The results, in my experience, with the treatment of acute and subacute eczema of the moist variety have been uniformly good with staphylococcus stock vaccine. Two hundred million each of staphylococcus aureus and albus is given for the first inoculation and subsequently increased if necessary. Inoculations are made at four to six days apart. Usually four to six doses are sufficient, but in two cases which came under my care ten doses were given before a cure was effected.

CHRONIC ECZEMA.

My early experiences in the treatment of chronic eczema in both adults and children were, as a whole, failures and this was essentially due to my adhering too closely to bacterial findings in selecting a vaccine. In many bacterial examinations made from cultures secured from skin scrapings after removing scales or scabs I uniformly found staphylococci, but never streptococci. From this I concluded that staphylococcus vaccine was indicated, and used both stock and autogenous preparations in small and large doses at long and short intervals, but only with temporary improvement. It was through Dr. Wolverton, of Badger, Iowa, however, with whom I was in correspondence at the time,

that I began to use vaccines which contained organisms that were not found by bacterial examinations with better results.

Dr. Wolverton reports the following experience (Bacterial Therapist, February, 1913):

"There is one pathogenic condition in the treatment of which the use of bacterins has apparently received but scant attention; I refer to eczema.

"About two years ago, a detail man from the biological department of one of the great pharmaceutical concerns visited me at Linton, N. D., at which place I was at that time located. He asked me whether or not I was using 'vaccines' in the treatment of eczematous conditions. I replied that such an application of the bacterins had not occurred to me, whereupon the detail man told me of a case that had come under his notice in Aberdeen, S. D. A woman of that city had for many years suffered from an eczema which had been treated by a number of competent physicians, with but slight and only temporary relief. The case finally came under the care of a physician (Dr. McCauley, I believe) who was interested in bacterial therapy. At first the doctor treated the woman by the use of ointments, alteratives, etc., with about the same lack of success which had crowned the efforts of his predecessors in the case. Then it occurred to him to make a culture from the eczematous crusts; this he did, and found the usual pyogenic cocci. From the cultures he prepared an autogenous bacterin, with the result that after a very few inoculations the woman was cured.

"Now, I had, and still have all the paraphernalia necessary for the making of autogenous 'vaccines,' but the various processes take up too much time to be practicable for the general practitioner. And I had had such excellent results from the use of polyvalent stock bacterins, in other pathologic conditions, that I decided to 'try out' the effect of a stock bacterin, containing the streptococcus pyogenes, together with a staphylococcus aureus et albus, in a case of chronic eczema which was under my care at the time.

"The patient was a little fellow of 5 years, who had been the victim of a stubborn eczema of the auricle, post-auricu-

lar and temporal regions, almost from birth. Treatment at the hands of three physicians (the last of whom was the writer) had given but scant temporary relief. So, on March 8, 1911, I injected into the subcutaneous tissues of the gluteal region a full cubic centimeter of vaccine containing streptococcus pyogenes 60,000,000 and staphylococcus pyogenes aureus et albus, aa 200,000,000, prepared by Dr. G. H. Sherman. Within the next twelve hours the eczematous patch became very red, and serum 'simply poured out,' to use the parents' words. Here I had used an unnecessarily large dose (I had given the full adult dose to a child of 5 years, but without any harmful results whatever, as you will see in a moment). The sluggish, chronic process had been lighted up into a very acute one. But in about 48 hours the flow of serum had gradually ceased, and rapid healing ensued. Eight days after the initial dose of bacterin, one-quarter the first dose was administered, and no local reaction resulted. At the end of two weeks, the observer had to look closely to detect the slightest trace of the old trouble. A complete cure had been effected at the end of a month. To maintain a high state of resistance, and so guard against a possible recurrence, 0.5 c.c. of the bacterin was administered on March 30, and again on April 14. No return of the trouble has taken place, to date.

"Another interesting case came under my observation last June. A 'peroxide blonde' waitress had an intractable scaly eczema behind each ear, and at the margin of the hair over her forehead. She had been referred to me by someone who knew of my work with the bacterins, but she was very pessimistic as to the results of treatment, as she said she had been given everything. I demonstrated to her the error of her statement by administering a dose of a combined streptococcus and staphylococcus bacterin. The patient was told to return in a week for a second inoculation but she failed to do so, and was not again seen until about six weeks later, when she walked into my office, to show me that she had been cured by that one inoculation.

"I could narrate quite a number of quite similar experiences, but time and space are limited, and these three case-reports will give some idea of how, after local applications and internal treatment have failed of results, a few inoculations of a mixed, polyvalent stock bacterin, containing the

common pyogenic bacteria which infest the skin, will often 'turn the trick.' "

After combining streptococcus and other organisms with the staphylococcus in my chronic eczema cases I soon got therapeutic results. I will cite an extreme case: This was a child 2½ years old. Her mother told me that the eczema started at the age of 6 months. When I first saw the child the entire body was covered and a major part of the skin was moist and raw. The mother informed me that the child had been under the care of a dermatologist and other doctors for two years without receiving any benefit. She was reluctant to try any more treatments because of the expense and the fact that the child was steadily growing worse. I persuaded the mother to give the vaccine treatment a trial and started treatment by giving polyvalent staphylococcus 100,000,000, streptococcus 10,000,000, pneumococcus 10,000,000, colon bacillus 20,000,000 stock vaccine.

Marked improvement was observed a few days after the first inoculation in that the child was not so restless, there appeared to be less itching, and the child slept better. The dose was gradually increased until seven times the original amount was given and inoculations were made at first five days apart and later at weekly intervals. In three months' time the child was entirely well, no sign of the eczema being left. Six months later the case relapsed with some appearance of the eruption on the back. Five inoculations of the same vaccine again cleared it up and after that the child remained well. Naturally such a result brought other cases of eczema in infants and children for treatment and in view of the similarity of the results a detailed report of the cases will be of no advantage.

In chronic eczemas of the hands, with cracks in the skin, the results have not been so good. It seems that in these cases the trouble is largely vocational, some irritating sub-

stances from the daily work or exposure to cold and moisture aggravating the condition and thus keep the skin from becoming normal. Where the patient is so situated that proper care can be taken of the hands, better results may be looked for. A recent case shows what can be accomplished:

Mr. M., traveling salesman. Eczema of both hands of twelve years' duration. Had both hands frostbitten and soon after developed eczema. Would clear up fairly well during warm weather but was always bad during the cold winters. He had been treated by many doctors and skin specialists but only obtained temporary relief. On account of this trouble he had contemplated making his home in the South. When cold weather set in the eczema again became aggravated. His father being a traveling salesman for a physicians' supply house and being somewhat familiar with the use of vaccines, inquired of me whether they were being successfully employed in cases of eczema. Treatment was started by giving staphylococcus 200,000,000, streptococcus 30,000,000, pneumococcus 30,000,000, colon bacillus 50,000,000. The dose was gradually increased to four times this amount, making inoculations at weekly intervals. He began to improve after the second inoculation. After eight inoculations his hands had cleared up.

Dr. H. H. Hazen (Southern Medical Journal, March, 1914) contends that most cases of eczema are either aroused or aggravated by the staphylococcus and has obtained very gratifying results with vaccines. He refers to a colored waiter who had suffered severely from erythematous eczema of the scrotum for nearly a year and was in bad physical condition on account of loss of sleep. Local and medical treatment gave no lasting benefit. After the third dose of staphylococcus albus vaccine the itching became less and after ten inoculations the eczema had entirely disappeared. He relapsed in two weeks, when vaccine

treatment was resumed and finally was cured, at least there was no reappearance of the infection six months after treatment was discontinued.

PSORIASIS.

Dr. Frank M. Wood, of Chicago, (The Urologic and Cutaneous Review, December, 1915, p. 680) reports four cases of eczema treated with vaccines and makes the following theoretical deductions:

"It may be a hasty generalization to assume that we have determined anything by our experiences in these four cases, but the results are, to say the least, very interesting and suggestive. Our view of the underlying causes of eczema, based on studies of this character, may be stated as follows: Eczema is an anaphylaxis of the skin due to the action of bacterial endotoxines on the vaso-motor nerve endings in the skin, most often caused by the toxines of the streptococci. A similar anaphylactic state occurs, with greater intensity, during the rash of the various acute exanthemata, when the lysis of the bacteria causing them takes place and their toxines are thrown in large amount into the serum at that time. In our first treatments of the staphylococcic dermatitis, we employed the vaccine made from the staphylococcus, because the staphylococcus alone was to blame for the process. In this last case, however, the staphylococcic vaccine made from the pustules caused the clearing off of the pustules, but the underlying eczema persisted. We then were led to investigate the gums. We then discovered the abscessing incisors, and the use of the streptococcus vaccine prepared from this focus brought the eczema completely under control.

"There are two remedies which we use in connection with the vaccines. Calcium lactate aids in checking the severity of the rash after the dose of vaccine is used, and is given in 8-grain doses every four hours, beginning on the day following the dose of the vaccine, and continued for two days. If the case shows any symptoms of anemia, the cacodylate of sodium given in $\frac{1}{8}$-grain doses hypodermically, alternately with the vaccine at the three-day or five-day interval, will act not only as a hematinic, but also as a

stimulator of the complement forming action of the leucocytes.

"When investigating infantile eczema, it is well to look first into the milk being ingested for streptococci. Breast milk and cow's milk may contain them. Abscess of the breast and fissured nipple are common in nursing mothers, and the streptococci may be found; if so they may also be found in the stools of the child. Garget is common in milch cows, and is all too common a source of the infective diarrheas of infants. The streptococcus mucosa, or the virulent capsulated streptococcus, is found in those infections following garget. Another source of repeated infections of this character in infants is enlarged tonsils and adenoids. The naso-pharynx in these cases will very often be found swarming with streptococci. But aside from these infections, possibly often following them, we find developing in many cases the inability to digest the heavy curd of cow's milk. This is a third form of eczema due to the non-split proteid of the cow casein. The obvious indications in such cases are elimination by the use of enema, followed by calomel to rid the gastrointestinal tract of the offending proteid, and the regulation of the diet. The latter may be accomplished by giving a milk in which the cream has been eliminated for a time at least, and by partially splitting the curd by the use of sodium citrate, diluting, if need be, by the use of the cereal waters which aid in the complete digestion of the curd. In every case where streptococci are found either in the stools, the milk or the naso-pharynx, it is well to employ the autogenous vaccine in small doses. The initial dose may be 5,000,000 cocci given at three-day intervals, and increased to 10,000,000 as the digestion improves. As a rule the food intoxication will clear up rapidly under diet, and clearing of the gastro-intestinal tract, but the more persistent cases may require the autogenous vaccines."

Like many other advances in medicine, the advantages of employing vaccines for eczema and psoriasis were discovered by some physicians by chance. Jesse W. Fisher (New York Medical Journal, Sept. 6, 1913, p. 469) believes in the importance of predisposing factors in eczema and is strongly of the opinion that where organisms can be found from pustules or from scales and exudate, bacterins are

valuable adjuncts in the treatment. The doctor reports the case of a patient—referred by Dr. Murphy, of Middletown, Conn.—who had suffered from eczema for years. He received bacterin treatment for furunculosis and as a result of this treatment his eczema also disappeared and had not returned in a year.

An obstinate case of psoriasis that came under my care about four years ago deserves special mention: This was a young man, aged 22. He had been treated for his psoriasis for over two years but was steadily getting worse. Both legs and arms were badly covered and some patches appeared on the body. Some spots were also starting on the face. All other treatment was discontinued. I gave him 0.3 c.c. of a mixed vaccine containing staphylococcus aureus and albus each 800,000,000, streptococcus 100,000,000, pneumococcus 100,000,000, colon bacillus 200,000,000 per cubic centimeter, and gradually increased the dose to one cubic centimeter, making inoculations at weekly intervals. He began to improve soon after using the vaccine in so far as the itching was concerned, but the lesions disappeared slowly. This was the only treatment, however, he had received that gave any prospects of ultimate success so he continued to come regularly; in six months most of the patches had gone. He was also much improved in his general health. After the dose had been increased to one cubic centimeter of the mixed vaccine the staphylococcus combined vaccine, 600,000,000 each of aureus and albus per c.c. was given alternately with the streptococcus, pneumococcus, colon combined suspension at weekly intervals, gradually increasing the dose to one and a half cubic centimeters of each. Later on the dose was extended to two-week intervals. After treating him a year he was free from his psoriasis. I have occasion to see the young man frequently, so his condition can be observed. It is now two years since treatment was discontinued and he is still free from his skin ailment.

Dr. Estelle D. Holland, of Hot Springs, Ark., (Journal A. M. A., March 13, 1915) reports three cases of psoriasis treated with vaccines for other ailments in which the psoriasis also got better. One case, Miss F., aged 32, had psoriasis on arms, chest and neck, was very miserable, had to wear high neck and long sleeves all the time and had gastric hyperacidity and catarrhal enteritis, for which she was treated by washing stomach, and used local treatment for the psoriasis. Five weeks later she caught cold and tonsillitis. The psoriasis got worse. An autogenous vaccine was prepared from organisms prepared from the throat, and stomach washing was discontinued on account of pain on passing tube. After three doses of vaccine the psoriasis was much better and in three weeks went home entirely cured. Eight months later she was still entirely free from the trouble.

Mr. B., aged 50. Patient had aortic regurgitation, lumbago, and psoriasis. Was sent by attending physician for baths. Four weeks' treatment with baths and medicine showed no improvement. Was put on a mixed vaccine streptococcus pyogenes 200,000,000, staphylococcus combined 800,000,000, and micrococcus catarrhalis 100,000,000 per cubic centimeter. The patient at that time had psoriasis on legs, arms, head and face. Much of his hair was lost. After sixteen days of vaccine treatment the patient left for home. By this time the psoriasis had stopped scaling and itching and was entirely eliminated except for the erythematous spots where the lesions had been. Heard from the patient six months later and at that time the psoriasis had not reappeared although he was not taking special care of himself and worked every day.

Mr. M., aged 38. A case of psoriasis of four years' duration lately became much worse, extending over arms, legs and body. In view of the results from the previous two cases with vaccine, the case was put on the same vaccine

treatment. He began to feel better after ten days' treatment and left for home in five weeks without a blemish.

Dr. Holland is testing out this method of treating psoriasis on a larger scale and no doubt will report results later.

ERYTHEMA.

Erythema may be ascribed to some irritation of the skin, such as woolen underwear, want of cleanliness, excessive perspiration, etc. Some persons have a thin skin and with such people slight provocations are liable to result in skin irritation, especially so if they are inclined to be corpulent.

Any skin irritation is liable to be aggravated by staphylococci normally present in the skin. If the immunizing resistance to the staphylococcus happens to be low, extensive inflammation with small superficial pustular eruption is liable to take place and continue to be annoying for a long time. Chafings during hot weather annoy some people very much. In infants the thin skin in the deeper folds caused by fat deposits under the skin are often very difficult to control by local applications and cleanliness. In all these conditions staphylococcus infection is the principal factor that prolongs the inflammatory condition. A staphylococcus aureus and albus combined vaccine will do a remarkable amount of good in all these cases. Treatment should be started by giving 200,000,000 and increasing the dose as indicated by reactions to 1,000,000,000 organisms. Inoculations should be made at five to seven-day intervals. Infants should receive proportionately less.

SYCOSIS.

Sycosis is in most instances caused by staphylococcus although streptococci are in some cases also responsible. For this reason, in the absence of a bacterial examination, it is advisable to give a combined streptococcus, staphylo-

coccus vaccine in these cases, and being of a rather acute condition, inoculations are made at somewhat shorter intervals, three or four days apart. The initial dose should be staphylococcus 200,000,000 and streptococcus 30,000,000. The dose may be increased to 1,000,000,000 staphylococcus and 100,000,000 streptococcus. In my experience the results have been very good. The pus should dry up after two or three inoculations, but it is advisable to continue treatment for two or three weeks after the lesions have cleared up to make the results more permanent.

URTICARIA.

Typical urticaria so often follows hypodermic serum administrations when employed therapeutically or prophylactically that the association of this disease with some sort of an anaphylaxis is quite logical. The disease has long been considered as being due to digestive disturbances. It is now believed that where urticaria follows after taking certain kinds of food, the protein in the food was absorbed without being properly digested and is then split up by ferments in the tissues of the body just the same as the protein of the horse serum contained in a dose of antitoxin is split up and followed by urticaria. Laxatives and various kinds of tonics have been recommended, but in some cases such treatment has given only temporary relief.

The tonic influence of a combined colon bacilli, streptococci, pneumococci, staphylococci vaccine on the digestive organs is very marked, and the good results gained in the treatment of urticaria with vaccines may be explained on the ground that the digestive functions are by this means stimulated to a point where the food is completely digested so the protein no longer enters the circulation in an unprepared state. I have seen some excellent results in cases of urticaria with the use of such a combined vaccine given in the usual doses at five or seven-day intervals. Dr. A. E. Owens, of Princeton, Ill., in a private communication relates the following interesting case:

"This case had been running for about three months, being constantly under the care of a physician and having experienced no relief from the trouble, in her discouragement, had decided upon a trip to the Carlsbad Springs. The patient made a visit to our town before taking her expected departure and upon her arrival she suffered an unusually severe attack and I was called to try to give her some temporary relief. Upon being informed by her of the men who had had her case in charge, and of the methods they had employed, I decided that nothing that I could do in the way of drug or dietetic treatment would bring her more relief than she had already received. I suggested to the patient that it was probably a case of colon bacteriemia and urged the use of colon bacillus vaccine. She was ready to accept any treatment that would at all promise relief. I gave her at once 40,000,000 colon bacillus vaccine with the result (this being in the evening) that the next day she experienced very little trouble from her disorder. This initial dose was followed in three days by a second dose of like size with the result that on the following day her trouble had practically disappeared. She was then obliged to return to her home in Chicago and requested that I give her a prescription for the vaccine that her physician might follow the treatment for a time and this was done. Unfortunately the dose that was given seven days after the second dose by her home physician, contained 100,000,000 bacilli. This dose produced an overstimulation with the result that on the following day she had a return of her trouble in a most aggravated form. The symptoms, however, subsided on the following day and up to this time, now about four months, there has been no return of the trouble."

RINGWORM.

Dr. A. Strickler (Journal of Cutaneous Diseases, New York, March, 1915, p. 161) after seven months' experience concludes that tinea tonsurans can be cured with vaccine.

He says not enough cases have been treated by this method to be, in the absence of other treatments, conclusive, but should at all events be a valuable adjunct to local treatment. He thinks from the results obtained this treatment should be placed at par with the X-ray method without the dangers that are associated with the X-ray treatment.

The cultures were obtained by selecting suspicious hair from three tinea tonsurans patients. To free the hair from contaminating organisms they were suspended for fifteen minutes in absolute alcohol, then immersed in sterile salt solution and planted, under aseptic precautions, into French proof agar in an Erlenmeyer flask and allowed to grow for 24 days. The growth was then triturated by rubbing it up with chemically pure sodium chloride crystals until the mass was sufficiently fine so it could be used without separating out the larger particles by filtration. Sufficient sterile water was added to make a normal salt solution of the water in the suspension. An ordinary Erlenmeyer flask yielded enough growth to make 500 c.c. of suspension. Eight to ten cubic centimeters of chloroform was added and heated to 60 C. for one hour to kill the growth. After this sterility tests were made on French proof agar. As a preservative, 0.25 per cent phenol was added and then tubed ready for use.

The vaccine was given hypodermically in the usual way in doses ranging from 0.5 c.c. to 2 c.c. There were no constitutional reactions from the vaccine, but after six or seven doses there would be some infiltration at the site of inoculation which would rapidly subside, especially so if painted with iodine. The number of injections varied from 7 in some cases up to 17 in others.

To my mind, any result gained from a vaccine prepared from a growth of an organism like the tinea tonsurans is assurance that antibody production destructive to almost any infecting agent may be expected by injections of the

killed suspension. The infection has the characteristic of being distinctly localized. That local immunization develops at the site of infection is clear from the fact that the infection gradually dies out at the point of original invasion but continues to advance by enlarging the ring. If systemic immunization would develop, this steady advance of the infection would not be possible. The local infection does not make sufficient impression to cause systemic immunity, but it appears that inoculations of vaccines prepared from the organisms does.

CHAPTER XIV.

BLOOD INFECTIONS.

Blood infections are evidently much more common than was at one time supposed. From the lessons taught by a more careful study of infections in various parts of the body as a result of focal infections it is evident that the infecting organisms are conveyed to the remote organs by means of the circulating blood. In such cases, however, the germs are present in the blood in such limited numbers and in all probability only for such short periods of time that the procuring of the organism by blood culture becomes problematical.

In cases where a more extensive blood infection exists a culture may be obtained by withdrawing 10 c.c. of blood from a vein with a sterile hypodermic syringe after having thoroughly sterilized the skin over the vein, and then planting the blood under aseptic precautions into tubes of peptone beef tea, with about one part of blood to five of peptone broth. A few drops of blood should also be planted on ascitic agar slants. The broth tubes and agar slants should then be incubated and examined for growth by the usual methods.

Rosenow (Journal A. M. A., Sept. 12, 1914) finds that in the less acute cases of blood infections where the organisms cannot be found by the usual methods they may be obtained by a method devised by himself as follows:

"In order to furnish bacteria from the blood and other sources a gradient of oxygen pressure, the following method for making blood-cultures has been used with good results: From 15 to 30 c.c. of blood are withdrawn from the vein at the bend of the elbow in the usual way and decalcified, by adding it to a solution of 2 per cent sodium citrate in sodium chlorid solution in the proportion of 5 c.c. of blood per 1 c.c. of solution. Control tests have shown that the bacteria contained in the blood from a wide range of conditions live

in this solution for at least 72 hours. The citrate solution is kept in a tube of suitable size closed by an aluminum screw-top containing a rubber disk and sealed with paraffin. This may be used at the bedside and then sent to the laboratory for cultures in case, for some reason, it is not convenient to make the complete culture at the bedside. In my work a portion of the citrated blood has been at once planted to sterile distilled water contained in bottles which serve as certrifuge tubes, there being at least 10 parts of water to 1 part of citrated blood. This is centrifuged at once and the supernatant hemoglobin containing water is poured off or the sediment removed with a sterile pipet, and planted. The sterile water serves as a means of getting rid of the hemoglobin and the serum. Control tests with the serum after the corpuscles have separated by gravity show that in the aerobic cultures the inhibiting action of the hemoglobin is more marked than that of the serum; in fact, the serum is a desirable constituent in streptococcal cultures. Hence in suspected streptococcal infections the serum and the sediment of the dissolved corpuscles may be planted separately. In some instances the hemoglobin has been converted into methemoglobin by passing carbon monoxid (illuminating gas) through the decalcified blood by means of a sterile pipet containing a long sterile cotton plug."

Of the various infecting organisms found responsible for blood invasions the streptococcus, staphylococcus, pneumococcus, and gonococcus are the most common. Among the less common organisms found in the blood the colon bacillus, influenza bacillus, typhoid bacillus, meningococcus, and bacillus pyocyaneus may be mentioned.

The presence and maintenance for any considerable time of an infecting organism in the blood is evidence of itself that the immunizing resistance to such an organism is low, and clinical experience seems to indicate that where an organism has once established itself in the blood stream it is liable to maintain itself until the infection localizes in some tissue with a resulting localized inflamed area. In pneumonia the pneumococcus circulates freely in the blood

at the time of the initial chill and disappears from the blood as lung consolidation develops. In cases of pyaemia staphylococci are found in great numbers in the blood until localized abscesses have developed, when the blood will clear up if the patient survives the infection. Puerperal sepsis is particularly dangerous when no localized inflammation develops. In typhoid fever, typhoid bacilli are most abundant in the blood during the early stages of the disease and become less as localized infection develops in Peyer's patches. Certain types of streptococci will maintain themselves for months in the blood and will only disappear from it after producing rheumatic joint, heart or other localized involvements. This indicates that adequate antibody production requires tissue involvement in the infective process.

Germ destruction in the blood takes place either by lysis or phagocytosis. Lysis demands the presence of ferments in the blood that dissolve the germs. Sir A. E. Wright demonstrated that phagocytosis is only possible when the leucocytes are suspended in a blood serum that has a sensitizing influence on the germs and that this sensitizing influence depends on some soluble substance present in the serum which combines with or attaches itself to the germ, and that in all probability the major portion of the germs present in the blood stream are destroyed by the leucocytes after they have become sensitized. Since adequate germ destruction in the blood does not take place until the infection localizes, it is quite clear that these sensitizing substances are mainly produced as a result of tissue involvement. The germ while present and multiplying in the blood evidently possesses a certain virulence which would involve some danger to the leucocytes if they were to ingest them and as a result the leucocyte retreats instead of making an attack. In other words, the germ in its attempt to live must digest and assimilate food. Digestion depends on the presence of ferments. The germ evidently surrounds itself

with an extracellular substance which possesses a digestive influence on substances with which it comes in contact, and the leucocyte, not being able to contend with an organism which possesses such destructive properties, refuses to ingest it. When the infection becomes localized the germs still possess their destructive properties, but the germs in this instance become anchored to the locality and their influence on the tissue cells becomes more continuous. Some of the cells at the center of infection may become destroyed, resulting in pus formation, but the constant influence of the localized infection is liable in time to develop the defensive mechanism with the production of specific ferments or antibodies. These ferments gain entrance to the blood stream and combine with or neutralize the destructive substances which surround the germ. When a germ is thus influenced its digestive apparatus is crippled and is then said to be sensitized. The leucocyte can then ingest it without danger to itself and in the process of digesting or dissolving the germ the leucocyte secretes a ferment which will also have a destructive influence on other germs of the same kind still circulating in the blood.

That the immune substance links with the germ and renders it an easy prey to the leucocytes may be readily demonstrated by suspending live virulent germs in immune serum for some hours, and then mixing them with leucocytes and blood serum, and incubating. It will be found that the germs are then an easy prey to the leucocytes. Furthermore, by suspending a sufficient number of germs in immune serum and then removing the germs by filtration or by precipitation with a high speed centrifuge the serum will no longer possess this property of sensitizing the kind of germs to which the animal that furnished the serum was immunized. This would show that the antibody present in the serum hitches to the germs, becomes an inseparable

part of them and that by separating the germs from the immune serum the antibody is removed from the serum with the germs.

From this it is clear that, in cases of blood infections where germs circulate freely in the blood, tissue sensitization for antibody production is most important and that such tissue sensitization does not take place for adequate antibody production until the infection localizes, causing tissue involvement. Here is where bacterins solve the problem. The killed organisms when injected under the skin rapidly sensitize tissue cells for antibody production. These antibodies gain entrance to the blood and there by combining with the germs devitalize or opsonize them sufficiently to let phagocytosis take place; and by repeating the inoculations enough tissue sensitization with antibody production is developed to eliminate the infection.

SEPTICAEMIA.

In cases of blood infection by the more virulent types of streptococci as a result of puerperal infection, infected wounds, severe tonsillitis, or some other foci of infection associated with high fever and other toxic symptoms, early vaccine treatment is of great importance. For this reason a polyvalent stock streptococcus vaccine should be given at once and in sufficient dosage. The initial dose should be from 60,000,000 to 100,000,000 streptococci. In the more severe type it is well to repeat the inoculation the next day. As a rule a marked drop in temperature, a better pulse, associated with a less anxious expression and other improved nervous symptoms, will be observed within one or two days. If not much improvement should be observed another inoculation of a somewhat larger dose should be given the third day and after that inoculations are preferably made at two or three-day intervals until the temperature becomes normal.

In case marked improvement does not take place from the first few inoculations of stock vaccine an autogenous vaccine prepared from the blood cultures should be employed. This practice at least gives the patient the benefit of the possibility that an autogenous vaccine may be of benefit if the stock preparation should fail. In my experience, however, vigorous treatment with stock vaccines will give excellent results if treatment is started early, but if the infection is allowed to progress until the patient's vitality is exhausted before vaccine treatment is instituted not much can be expected from either stock or autogenous vaccines.

PYAEMIA OR STAPHYLOCOCCUS BLOOD INFECTION.

The staphylococcus is characteristic in its tendency to cause prolonged infections, because the live organism possesses poor antigenic properties in the presence of an infection; and this is particularly the case when the organism gains possession of the blood current. Furthermore, even when the infection localizes with abscess formation, tissue sensitization for antibody production develops very slowly, with a resulting extensive abscess development, prolonged illness or final fatal termination. On the other hand, killed staphylococci when injected under the skin possess marked antigenic properties. A single dose of staphylococcus vaccine will be instrumental in stimulating more antibody production, as shown by clinical improvement, than would develop from extensive tissue involvement by the live organism.

For this reason some of the most striking results in vaccine therapy are obtained by giving staphylococcus vaccine in cases of pyaemia, especially if treatment is started early, before localization with abscess formation has taken place. The initial dose should be 400,000,000 of a polyvalent stock staphylococcus vaccine, and the dose repeated at daily intervals for two or three doses. After the temperature

drops and other conditions improve, the intervals between inoculations should be extended to three or four days and the dose increased to 600,000,000 or 800,000,000. If abscesses develop they should be promptly drained. Unless vaccine treatment is started entirely too late and proper surgical treatment is neglected, uniform good results are gained.

ENDOCARDITIS.

Endocarditis is probably always preceded by a blood infection, but the incidence of heart infections does not appear to have any relation to the virulence of the infecting organisms. In fact it appears that the very virulent types are not as liable to cause localized heart lesions as the less virulent ones. This appears to be particularly true of the various streptococci. Streptococci are by all odds most frequently responsible for endocarditis, but pneumococci, staphylococci, influenza bacilli, gonococci and other organisms are also occasionally found.

Drs. Oille, Graham and Detweiler, of Toronto, (Journal A. M. A., Oct. 2 1915, p. 1159) point out that endocarditis with an accompanying blood infection is of more common occurrence than is usually supposed. They find that by employing Rosenow's method of blood culturing, streptococci are often found where the usual methods of blood examinations prove negative. They also find that cases with a slight rise of temperature probably several times a week with obscure symptoms of infection, but no local manifestation of a focal infection, frequently have a blood infection with endocarditis.

Endocarditis may present an endless variety of severity. Many cases with slight lesions recover entirely. I have in mind a girl eight years of age who had a severe attack of inflammatory rheumatism with a heart involvement which gave a distinct mitral murmur for six months. It finally cleared up entirely and although twenty years have passed

she is enjoying perfect health, never having had the slightest trouble with her heart since. There is good reason to believe that there are many similar cases.

Concerning the vaccine treatment of an active endocarditis associated with a blood infection, several difficulties are encountered. In many of these cases the infection is of somewhat long standing. Rosenow (Journal A. M. A., November 10, 1910) points out that as a result of this prolonged infection the germs develop a certain resistance to the immunizing activities of the host, so that the leucocytes can no longer ingest and digest them effectively. As, in the case of other chronic infections, a certain tolerance to the infecting organism is established. Furthermore, in time, vegetative enlargements develop at the focus of infection which cannot be dealt with surgically and meantime the infected focus becomes walled off, so a free blood supply is excluded from the actual focus of infection and consequently even if immunizing substances are present in the blood the germs at the focal infection can not be effectively reached. With germs constantly pouring into the blood stream from such a focus, naturally the blood can not become sterile.

From these considerations the importance of early immunization is perfectly apparent. Early in the course of an infection, before this mutual tolerance between tissue cells and infecting organisms has developed, much more striking results from the use of vaccine inoculations are gained than in the chronic variety. This would largely account for the fact that better results are obtained from the use of bacterial vaccines in acute pyaemia and septicaemias than in these subacute types of blood infections. And in considering early vaccine treatment I do not wish to convey the idea that to institute vaccine inoculations after permanent damage has been done to the heart, constitutes early treatment. It is now well recognized that most cases of endo-

carditis have their origin in a tonsillitis, usually as the result of a streptococcus viridans infection. Vaccine treatment should start right at the tonsillar infection and not after the blood and heart have become involved, if the best results are to be obtained. The same principle holds good with an endocarditis due to a gonococcus, staphylococcus, pneumococcus, or any other infecting organism. If the original focus of infection is treated by therapeutic immunization sufficient systemic resistance will develop to prevent a blood invasion. In all my experience with the use of vaccines I cannot recall a case in which an endocarditis developed as the result of a focal infection where vaccines were employed in its treatment before the heart infection took place.

Autogenous vaccines have been extensively employed in advanced cases of endocarditis, but from the reported cases the results have not been encouraging. A temporary benefit has been noticed in most of the cases, but permanent, beneficial results only appear to be secured in moderately advanced or early cases. These indifferent results, in my judgment, are at least in a measure due to the tolerance that the patient has developed to the organism from which the autogenous vaccine is prepared. In chronic infections I have for the same reason frequently found that polyvalent stock vaccines give results where autogenous preparations have failed. If the infection has done sufficient damage to the heart valve to materially cripple the function of the organ, vaccines can do no material good. Even if the infection could be overcome in such a case death would eventually intervene as the result of a crippled heart.

CHAPTER XV.

INFECTIONS OF THE GENITO-URINARY SYSTEM.

General Consideration.

Infections of the genito-urinary system are common and varied. Aside from tubercle infections we find that practically all the common pyogenic organisms found in diseased conditions of other parts of the body may also be either the direct or indirect cause of urinary affections, and in addition to these the gonococcus must be added as the most frequent primary invader. The importance of means for efficient treatment by the early elimination of infections of the genito-urinary system can be thoroughly realized when we consider that by crippling this system the principle organs of elimination and the organs of regeneration are put out of commission. The inadequacy of drugs in the treatment of genito-urinary infections is well recognized, and from present day experience it appears that therapeutic immunization with bacterins offers the only hope of effectively taking care of these cases. Every practitioner knows the dangers of a nephritis under conventional treatment. Drugs and local treatments in cystitis, urethritis, prostatitis, epididymitis, orchitis, salpingitis, metritis, etc., fail too often to offer much encouragement for these methods. Drugs and local measures when properly applied are of great value and while employing bacterins such other measures that are of known advantage should not be neglected, nor should a stricture, urinary calculus, a pus cavity or other surgical condition be treated without proper surgical interference.

Acute and Chronic Nephritis.

On the question of nephritis two conceptions prevail: (a) that toxic materials eliminated from the body by the kidney cause an irritation with a resulting inflammation of the kidney tissue, and (b) that in active inflammation of

the kidney, the kidney itself is infected. That irritating substances eliminated by the kidneys do cause kidney inflammation is well illustrated by cases of bichloride poisoning, excessive doses of carbolic acid, urotropin, lead poisoning, etc., but we find that such cases recover rapidly if the specific poison is disposed of. When a nephritis supervenes in a case of acute infection it is believed by some that toxic substances evolved as a result of the infection and eliminated by the kidney have a similar irritating effect on the kidney structure.

From my general conception of the inflammatory influence that pathogenic organisms have on infected tissues and from my constantly finding pathogenic bacteria in the urine from cases of nephritis I have for a long time been of the opinion that nephritis is the result of kidney infection.

The bacteriology of the urine in health and disease has been extensively studied. To arrive at a positive conclusion whether or not the urine is sterile in health is surrounded with some difficulty because staphylococci are usually present in the urethra. So, even when a specimen is collected by catheterization, there is always a chance of urethral contamination, but the number of organisms from such a source are always small, and when a considerable number of germs are found in the urine is is safe to assume that the organisms are present in the urine.

Some of the most recent work on the bacteriology of urine was done by Drs. George F. and Gladys R. Dick (Journal A. M. A., July 3, 1915, p. 6), who, to avoid contamination, collected the urine by catheterizing the ureters. Cultures of 2 c.c. of catheterized urine were made in deep tubes of dextrose agar; aerobic and anaerobic cultures on blood ascites agar were made from the sediment of 15 c.c. of centrifuged urine.

The results of their work is most aptly compiled in their table as follows:

THE INCIDENCE OF VARIOUS ORGANISMS FOUND IN THE URINE IN HEALTH, FOCAL INFECTIONS WITHOUT NEPHRITIS AND IN NEPHRITIS

Case Number	Diagnosis	Organisms Found in the Urine																
		Staphylococcus	Pseudodiphtheria	Gram-positive Anaerobic Coccus	Gram-negative Spore-forming Aerobic Bacillus	Gram + Barred and Beaded Aerobic Pleomorphic Bac.	Anaerobic Gram — Diplococcus	Strepto-Bacillus	Large Gram + Anaerobic Bacillus	Diplococcus Catarrhalis?	Gram + Spore-forming Bacillus, Aerobic	Streptococcus	Diphtheria Bac.	Small Gram + Anaerobic Bacillus	Small Gram — Anaerobic Bacillus	Spirillum	Pigment-forming Bacillus	Small Gram — Aerobic Bac.
1	Health		+															
2	Health	+																
3	Health																	
4	Health																	
5	Chr. appendicitis	+										+						
6	Diabetes mellitus, pyorrhea alveolaris	+						+										
7	Acute articular rheumatism; pyorrhea alveolaris				+							+						
8	Tuberculous arthritis; secondary infection	+										+						
9	Ethmoidal sinusitis		+							+		+			+			
10	Acute nephritis														+			
11	Acute nephritis																	
12	Acute nephritis											+	+					
13	Acute nephritis	+	+?									+						
14	Acute nephritis	+										+						
15	Acute nephritis					+												
16	Acute nephritis											+						
17	Chronic nephritis		+									+		+				
18	Chronic nephritis											+						
19	Chronic nephritis		+	+											+			
20	Chronic nephritis														+			
21	Chronic nephritis		+				+							+				
22	Chronic nephritis	+										+		+				
23	Chronic nephritis	+							+					+				
24	Chronic nephritis																	
25	Chronic nephritis	+										+			+			
26	Chronic nephritis		+									+						
27	Chronic nephritis					+					+							
28*	Chronic nephritis											+			+	+	+	
29*	Chronic nephritis											+			+			+

* Cases of previous report.

A study of their work shows that the urine in health is for all practical purposes sterile, only one colony of pseudodiphtheria bacillus being found in case one and eleven colonies of staphylococcus in another case. It will be observed that the streptococcus is the most common known pathogenic organism that was found in both the acute and chronic nephritis. They also found that in cases of coccus infections, organisms identical to those present in the infected focus may be also be found in the urine without the presence of albumin, casts or other indications of kidney disease. This is in accord with the findings of other investigators and would indicate that the kidney is capable of eliminating live pathogenic organisms from the blood as it passes through the kidney.

Dodge (Journal Michigan State Medical Society, Feb., 1910) reports cases of focal infections treated with vaccines prepared from organisms isolated from the urine and contends that the kidneys eliminate organisms that gain entrance to the circulation.

The frequency with which streptococci are found in the urine in scarlet fever and micro organisms in typhoid, and other acute infections without albuminuria or other indications of kidney involvement is good evidence that germs may pass through the kidney without injuring it. The frequency with which nephritis follows scarlet fever shows, however, that streptococci may become active pathogenic agents in kidney inflammations. Rosenow (Journal A. M. A.), by inoculating rabbits intravenously with streptococci isolated from kidneys, found that 75 per cent of the rabbits thus inoculated showed kidney infection.

The fact that so many cases of nephritis date back to an acute infection is strong evidence that the kidney involvement is a sequence to such infection. These kidney infections are sometimes sufficiently acute to suspend the function of the kidneys and in a short time terminate fatally. Others will partially recover, lapse into a chronic state, with a resulting disintegration of the organ, prolonged illness and death. When the acute infection is not too severe, spontaneous recovery will take place. In many cases of nephritis the disease is insidious in its development and dates back to a "cold" or some other minor infection. In such cases it is quite clear that the kidney infection had its source from the infection which caused the "cold."

From these various considerations it is quite clear that nephritis is due to infection and that therapeutic immunization is indicated. In this connection I wish to point out the importance of treating colds and other acute or focal infections by immunization and thus avoid a later kidney involvement. My experience, at least, justifies such a con-

clusion. So far no case under my observation developed a nephritis where vaccines were employed during the early stages of an infection.

My experience with bacterins in the treatment if nephritis is limited to ten cases. All were so extremely advanced that any improvement would indicate their therapeutic value. Of the three acute cases two adults were in a comatose condition from uremic poisoning when treatment was started. Stock vaccine was used while autogenous vaccines were being prepared and active elimination by sweats and cathartics was instituted. Both cases terminated fatally within ten days. They both lived longer than their condition would indicate when treatment was started.

The third case was a child three years old. The child took sick running a high fever with throat involvement. I suspected scarlet fever developing but at no time found the slightest rash. The urine became bloody with much albumin. On account of the difficulty of procuring the urine under aseptic precautions no bacterial examination was made. Stock streptococcus vaccine combined with colon bacillus was given at three-day intervals. The fever subsided after the first inoculation but while the bloody condition of the urine disappeared, albumin was present for about ten days. The child made a complete recovery. If there was any scarlet fever element in this it was not apparent.

My experience in the use of vaccines in chronic nephritis convinces me that none of these cases should be abandoned until vaccines have been given a fair trial. Naturally where the kidney tissues have become disorganized from a long continued infection not much permanent benefit can be expected, but where the kidney is still in a condition where repair is possible if the infection is eliminated, permanent good can be accomplished. The following cases illustrate what may be accomplished in some extremely bad cases:

Mrs. S., age 60, had been sick with nephritis for eight months. Six months of this time she had received treatment from competent regular physicians and two months of hydropathic treatment at a sanitarium consisting of sweats and baths, being restricted at the same time to an absolute vegetarian diet. She steadily grew worse and was sent home as a hopeless case. When I first saw her she was very dropsical, the whole body being swollen and only one-half pint of urine was passed in 24 hours. The first consideration was to relieve the dropsical condition for which pilocarpin was given to procure free perspiration and elaterium to produce copious watery stools. The next day a dose of streptococcus-colon bacillus combination vaccine was given and a sample of urine was procured under aseptic precautions for bacterial analysis. There was not much sediment, but colon bacilli were found in abundance. On boiling and precipitation with nitric acid, urine showed that one-half its volume was albumen. Her improvement after the first dose of vaccine was so marked that it was continued at five-day intervals for six weeks when she was feeling quite well, passing a normal amount of urine and the dropsical condition was almost entirely gone. The urine, however, still showed small amounts of albumen, so the treatment was continued regularly for a year during which large and small doses at long and short intervals were tried out, but the albumen still persisted in small quantities. Otherwise she felt entirely well. She received occasional inoculations of vaccine after that for several years, but I lost track of her after that. Recently, eight years after I first started to treat her she called at my office on account of some swelling of the feet which had been developing for a few days. She said that she had felt entirely well up to the time her feet began to swell. Urine examination showed a large amount of albumen likely due to a new infection of the kidney. A combined stock vaccine containing streptococcus, pneumococcus, staphylococcus, colon bacillus, was

given at once. Five days later she called again when the swelling of her legs was almost entirely gone, but there was still considerable albumen in the urine. The vaccine was repeated at weekly intervals and in six weeks' time the urine was almost entirely free from albumen. There is still some trace of albumen in her urine but clinically she is entirely well.

Mr. S. Had been ill for over a year. I knew the man well and frequently saw him during this time. For several months before my brother, Dr. A. T. Sherman, and I were called to see him, he had been under the care of a prominent regular physician. When we saw him he had been confined to bed for a month with frequent vomiting. For a week he had retained practically no nourishment. Eyesight much impaired, severe continued headache. Urine scant and cloudy, containing casts and much albumin. A distinct circumscribed enlargment could be mapped out over the region of the spleen or lower margin of the stomach which was considered as probably malignant with a possible chance of being an enlarged spleen. Bacterial examination of urine showed pseudo-diphtheria bacillus and staphylococcus aureus. An autogenous vaccine was prepared. The autogenous vaccine was not depended upon, however, so a stock vaccine containing streptococcus, pneumococcus, staphylococcus and colon bacillus was used alternately with the autogenous vaccine. Inoculations were made alternately at three day intervals, treatment being started with the mixed vaccine. The general condition of the patient soon improved and after two weeks' treatment his vomiting let up entirely, the headache was relieved, and the condition of the eyes was much improved. Urine examination also showed much less albumin. Five weeks after the vaccine treatment was started the urine showed only a very small amount of albumin. His appetite became good and his wife told me that he ate more than when he was well

and was able to digest what he ate. His eyes regained their normal sight, could sleep well and gained enough in strength so he was able to sit up. I observed that he always felt best after the mixed stock vaccine so the autogenous vaccine was discontinued. The patient continued to do well as far as the nephritis was concerned, but the malignant character of the enlargement in the region of the spleen became more pronounced. Several consultations were held but, on account of the advanced condition of the case, surgical interference was not considered advisable. He died four and a half months after vaccine treatment was started. No post-mortem was made, but all clinical symptoms indicated that he died from a cancer in the region of the spleen.

To my mind this is an interesting case, in that it points out what may be accomplished in the treatment of infections with vaccines under exceedingly adverse circumstances. Clinical symptoms showed that the nephritis was taken care of, but that death ensued from a malignant growth.

The following case came under my observation through my brother, Dr. A. T. Sherman, who treated the patient, while I occasionally took care of him during his absence from the city:

"J. P., male, age 38 years. Accountant, working in office most of the time. During the month of September, 1913, he had an acute coryza which lasted for several weeks. The following month he noticed that his face was swollen on rising in the morning. His appetite was bad, and he suffered with a headache almost constantly. A physician was consulted who prescribed some medicine, but did not examine the urine. After six weeks' treatment there was no improvement. The doctor then made an examination of the urine and found albumin. The patient was then put to bed and treated with hot packs three times daily for three months. The bowels were also flushed freely at frequent intervals with saline cathartics. A rigid diet consisting of rice, toast, tapioca pudding and buttermilk was

adhered to. No material improvement was noticed by the patient during this time. During the following four months he was up part of the time, took hot packs occasionally and cabinet baths daily. The original physician was continued in charge of the case with the aid of four different consultants. During all this time he was steadily growing worse.

"When he came under my care, June 20, 1914, the previous attending physicians considered him a hopeless case, and intimated that any hopes for a material improvement or ultimate recovery was entirely out of the question. His physical condition was typical of an advanced case of nephritis. The entire body was dropsical. The legs and feet were badly swollen, the abdominal wall was infiltrated and considerable fluid was present in the peritoneal cavity. Both arms and hands were swollen, and his face was so badly swollen that he opened his eyes with difficulty. He was very feeble, breathing difficult, and was scarcely able to walk. Pulse was irregular, but had fair volume. No heart lesions present. There was a retinitis present which interfered with his vision sufficiently so he could not read ordinary print. Headaches were almost constant. Twenty-four-hour urine amounted to ten ounces with specific gravity 1010. There was much albumin present, constituting about one-third the volume after being coagulated with heat and nitric acid and allowed to settle. Bacterial examination of the urine by cultural and microscopic methods showed colon bacillus, streptococcus and staphylococcus.

"I discontinued cabinet baths, hot packs and purgatives entirely. Also discontinued his rigid diet and advised a diet consisting of milk, raw eggs, vegetables and fruits. Vaccine treatment was started by giving 0.3 c.c. of a combined vaccine containing streptococcus 100,000,000, pneumococcus 100,000,000, staphylococcus aureus, albus and citreus, each 200,000,000, and colon bacillus 200,000,000 per c.c., from which no material reaction followed. Five days later 0.5 c.c. of the same vaccine was given. The dose was gradually increased to 1 c.c. At first inoculations were made five days apart and later on at weekly intervals. He began to show improvement after the second inoculation. After a little over three months' treatment the dropsy had entirely

disappeared, normal vision had returned, and his general health and strength had improved sufficiently so that he was again at work at his usual occupation. His urine became normal in quantity but still contained albumin. Treatment was continued for over a year but urine has not entirely cleared up. Otherwise he appears entirely well and feels well. He was re-elected treasurer of his county and attends to his duties regularly."

The other five cases all made some improvement after using the vaccines but lapsed back again and finally died. Autogenous vaccines prepared from organisms isolated from the urine were principally relied upon, but from later experience in the use of vaccines I believe that better results would have been obtained if mixed stock vaccines had been given a more extensive trial.

NEPHRITIS OF PREGNANCY.

Nephritis of pregnancy, from the literature on this subject, appears to be most frequently due to the colon bacillus, although pneumococci and streptococci have also been found in the urine of such cases. Medical treatment in these cases has certainly been most unsatisfactory. Therapeutic immunization promises the most satisfactory method of taking care of this condition.

Allen ("Vaccine Therapy," third edition, p. 147) says:

"In acute nephritis, and especially in the pyelitis of pregnancy, recourse should be taken to vaccine treatment when colon bacilli are present. It is, of course, well known that a bacteriuria tends speedily to clear up after evacuation of the pregnant uterus; but when acute symptoms appear in the third or fourth month it is better not to await delivery, but to employ a vaccine—a method of treatment which has yielded most successful results at the hands of some."

From our general knowledge of kidney infections and from the fact that streptococci are so liable to invade the kidney it would appear that a combined streptococcus, pneumococcus, staphylococcus, colon bacillus vaccine would

answer a better purpose than to employ a vaccine that contains such organisms only as are found in the urine. It does not necessarily follow that streptococci or pneumococci must be found in the urine if these organisms are present in the tissues of the kidney. Furthermore, these organisms are very liable to invade tissues that are inflamed by other causes and by including them in a vaccine the patient is being prophylactically immunized at the same time that the existing infection is being taken care of.

Some cases are found in which bacterial examination of the urine shows pathogenic organisms where no definite focus of infection is apparent. I have used vaccines in the treatment of some such cases and it may be well to mention a few of them:

A young man with previous good health complained of not feeling well. He had been losing in weight gradually and tired easily. He had no local pain and no urinary symptoms, slept and ate well but did not seem to relish his food as formerly. Chemical analysis of the urine showed nothing abnormal. Bacterial examination revealed staphylococci. Six doses of staphylococcus aureus and albus stock vaccine, starting with 300,000,000, completely restored his health.

A lady of middle age complained of pain in her knees and back, and general lassitude, want of vigor, and depression. This condition had lasted almost constantly for three years. The pain in her knees was considered rheumatic but otherwise there was no physical evidence of ill health. She had been treated by several doctors and had taken treatment and baths in a sanitarium. She informed me that examinations of the urine had been made and it was found normal. I procured some urine and found no albumen, casts or sugar but, strangely enough, a bacterial examination showed pneumococci and colon bacilli. A stock vaccine consisting of colon bacilli, pneumococci and

streptococci was given once a week. The streptococci were included for the rheumatic condition of the knees. She began to improve after the fourth inoculation and after fifteen inoculations was restored to her former health with the exception of some pain in her knees which was also relieved by continuing the treatment for six months. She was so pleased with the results of this treatment that she wished to continue it for some time, fearing that her trouble might return. She has recovered entirely.

A lady of previous good health consulted me concerning frequent urination during the night. She would sleep a short time then awaken with a pain in the head and a desire to void her urine. This would happen from eight to twelve times during the night. During the day she was not troubled so much. There was no evidence of urinary calculi; the urine was normal in quantity during the 24 hours, and a chemical examination showed nothing abnormal and there was little sediment. A bacterial examination revealed colon bacilli.

A stock vaccine was given at first but she was very sensitive to the vaccine and it produced considerable local irritation. An autogenous vaccine was made from organisms isolated from her urine and treatment was started with this vaccine. Twenty million of dead organisms were given for the first dose. Quite a local irritation was produced and the dose was not repeated for two weeks. Inoculations were then continued for eight weeks, the dose being gradually increased to 80,000,000, at which time her trouble had entirely ceased. About eight months later she noticed a return of the symptoms and I began to inoculate her again with the same vaccine. She still showed a slow resistance to the colon bacilli as evidenced by the amount of inflammation produced where the inoculation was made. Inoculations were continued for four months and gradually increased, but the desire to urinate at night was not entirely

relieved. Later on treatment was continued with a combined colon bacillus, streptococcus, pneumococcus, staphylococcus stock vaccine with better results, but the desire to frequently urinate during the night has not been entirely relieved.

PYELITIS.

Whenever pus is found in the urine a careful search for tubercle bacilli should not be neglected and where found proper specific treatment for a tubercle infection instituted. In the absence of a tubercular condition the usual infecting organisms are colon bacilli, streptococci, pneumococci, staphylococci, and occasionally the bacillus pyocyaneus. It is difficult to say just how the infection takes place, but in all probability in most instances the infection extends upwards from a cystitis. The same vaccine that is employed in the treatment of cystitis should here be employed.

CYSTITIS.

The bacteriology of cystitis has been extensively studied and it appears that in about 60 per cent of the cases the colon bacillus is the primary cause. In many cases, however, other organisms come in as secondary invaders, especially the staphylococcus, streptococcus, pneumococcus and the pseudo-diphtheria bacillus. The bacillus pyocyaneus, and Friedlander bacillus, are found in some cases. The gonococcus, in cases of gonorrhea, is also frequently responsible for bladder inflammation.

When making a diagnosis a stricture, an enlarged prostate and the possibility of a renal calculus or some other mechanical irritant being present in the bladder should always be carefully ascertained before vaccine treatment is instituted. The unexpected is sometimes found. Some twenty years ago I operated on a woman for a renal calculus and to my surprise found several well-preserved skull bones from a fetus in the bladder. The woman had an abortion several years previously, was sick for a long time and finally

recovered, but was left with a cystitis. The doctors who had charge of her case evidently never emptied the womb. The small skeleton bones probably passed by way of the vagina but the skull bones, being too large, ulcerated their way into the bladder, leaving a fistulous opening between the womb and bladder for a time which had closed at the time of operation.

I have used both stock and autogenous vaccines in cystitis. A sample of urine procured by catheterization under aseptic precautions offers a ready means of procuring the organism to prepare an autogenous vaccine after a bacterial examination by the culture method has been made, but my observations have led me to believe that unless unusual organisms are present a combined vaccine containing colon bacillus, streptococcus, pneumococcus, and staphylococcus gives the best clinical results.

The following case is a fair illustration:

Miss M., age 25, school teacher. Complained of tenderness over the bladder with frequent urination which had continued for two months. There was no evidence of the patient ever having had gonorrhea. Urine was cloudy and contained many colon bacilli. The combined stock vaccine referred to above was employed. She began to improve after the first inoculation and after six injections at five to seven-day intervals she made a complete recovery. It is now over a year since she received her last treatment and no symptoms of cystitis have returned.

Observers on the use of vaccines in cystitis are quite unanimous that this is the best method of treatment, but most of them contend that, while the clinical symptoms indicate a cessation of the inflammatory condition and urine examinations show a great reduction in the number of germs, in a majority of cases the germs do not entirely disappear. Emery ("Immunity and Specific Therapy,"

p. 394) says that vaccine inoculations cure the symptoms with a great reduction of pus and germs in the urine, but does not exterminate them entirely. He considers vaccine treatment the best available method of taking care of these cases.

I am convinced that failures in clearing up bladder infections are sometimes due to relying on autogenous vaccines prepared from the principal infecting organisms found in the urine. Autogenous vaccines are not always the best vaccine to use in a case, nor do we always get the best results by using only such organisms in the vaccines as are found in the infection. When autogenous vaccines are employed in treating cystitis all the pathogenic organisms found in the urine should be made up and the dose increased to large proportions. If the case fails to clear up a polyvalent mixed vaccine should be resorted to and given over a long period of time. In cases where the colon bacillus is the only organism present it is often found of advantage to include streptococci with the colon bacillus. There seems to be some relationship in the immunizing mechanism which makes a resistance to colon bacillus more effective when the immunity is raised to the other organisms as well as to the colon bacillus. Furthermore, a long-continued infection on a mucous membrane where the infecting organism is liable to develop a condition in which the germ can defend itself by becoming in a measure immune to the antibacterial substances that are formed as a consequence of the infection, naturally would not be as much influenced by antibodies that are developed from autogenous vaccine inoculations as from a polyvalent mixed stock vaccine where immunizing resistance is developed from various sources.

Infections of the bladder by the bacillus mucosus are not common, but extremely disagreeable when they do exist. One case, a doctor, came under my observation for such an

infection. His cystitis had been of some months standing, but was steadily growing worse. The mucous was formed so rapidly that there was almost a constant dripping of a mucoid substance. There was no history of ever having had gonorrhea. He began to improve soon after autogenous vaccine injections and in two months' time was cured.

ACUTE GONORRHEAL URETHRITIS.

The gonococcus is an organism that has a distinct tendency to cause subacute and chronic infections in which there is a slow development of an immunizing resistance. This has been clearly brought out by various investigators as a result of applying the complement fixation test as a means of determining the presence of a gonorrheal infection; complement fixation being obtained only in cases where gonococcus antibodies have been formed and found their way into the blood. These complement fixation tests show no positive reactions from cases of anterior urethritis or vulvo-vaginitis. A posterior urethritis may show a positive reaction during the sixth week. Deep-seated gonococcus infections like epididymitis, orchitis, or arthritis invariably give a positive reaction, and this may be obtained in about 50 per cent of prostatic cases. From this it is quite clear that a somewhat extensive, deeply seated gonococcus infection is necessary to develop a measurable amount of immunizing substances. Furthermore, an immunity that has become established soon wears off. Anyone who has recovered from an attack of gonorrhea is liable, when exposed, to again become infected and often the second attack is more intractable than the first.

Much controversy has arisen concerning the advantages of using gonococcus vaccine in the early stages of acute urethritis, some claiming great advantages from its use, while others contend that no advantages are gained. From a careful investigation of this subject I am convinced that opposition to the use of gonococcus vaccine in acute

gonorrheal infection is principally based on a theoretical opposition to the use of vaccines in acute infections for "fear of the negative phase," with a resulting insufficient dosage. That the antigenic or immuno producing properties of the gonococcus in a surface infection is nil is evident from the persistence of the infection and from the lack of a measurable amount of antibody production as shown by complement fixation tests. That killed organism injections do rapidly train or develop tissue cells for antibody production in the presence of an acute infection has been abundantly demonstrated and from experience we find that the earliest possible administration gives by far the best results. Gonorrheal infections are no exception to this rule if vaccines are given in sufficiently large doses and at proper intervals.

An occasional epididymitis after using vaccines has been ascribed to a negative phase and pointed out as one of the dangers following its use. In reply to such reasoning, Allen ("Vaccine Therapy," fourth edition, p. 247) aptly says: "No consistently good reports have ever reached me from the use of small doses of a gonococcal vaccine, whereas full doses rarely fail to produce a good result. Despite this, numerous workers are deterred from the use of adequate doses by the reports of two or three cases in which an epididymitis or a prostatitis followed very soon after the administration of a fair dose of vaccine. Surely the complications of urethritis are frequent enough when treated on purely orthodox lines to make any thinking person pause before ascribing the advent of the complication to the administration of the vaccine. It is equally open for the vaccine therapist to retort that in default of the inoculation the extension might have been more acute and more widely disseminated. It is, perhaps, not a correct attitude of mind, but as I believe I was the first worker on vaccine treatment as applied to acute gonorrhea, I cannot help feeling some resentment whenever I read the conclusions of those who perchance never used a larger dose than 5,000,000 that vaccine treatment is without effect on the course of an acute urethritis. Inasmuch as the essence of all vaccine treat-

ment is to use such doses as will produce local changes at infected foci, it necessarily follows that such observers were either working with an inert vaccine or were employing totally inadequate dosages. An extensive experience of the subject enables me to say that I have never yet seen a dose of 25,000,000 to 50,000,000 of gonococcal vaccine have any ill effect on the course of an uncomplicated urethritis, and I have very often seen it exert a marked influence for good."

Dr. Malcolm Dean Miller (The American Journal of Clinical Medicine, May, 1914), in referring to the use of vaccines in acute gonorrhea, says:

"Acute gonorrhea, however, seems to me to offer the best field for the use of bacterins. I have treated five male patients seen at the appearance of the 'first drop,' the initial doses being from 100,000,000 to 250,000,000 gonococci. As soon as the local reaction had subsided I doubled the initial dose, after which the symptoms almost entirely disappeared, no case going on to a profuse purulent discharge, or, in fact, there being experienced any more urinary scalding. After three or four doses, discharge being entirely absent, I have kept the patient under observation for several weeks and not terminated treatment until I obtained three successive negative tests, at weekly intervals.

"The average duration of discharge has been about seven days. The injection intervals average about one every third day, and I feel sure that I get the best effect by using 250,000,000, 500,000,000, and 1,000,000,000 microbes. My old teacher at Harvard casts doubt upon my results by saying that probably they were light cases; but I have never seen a case which cleared up in less than six or eight weeks under the irrigation-injection method."

In my conversations with physicians who contend that vaccines are not beneficial in acute urethritis I have found that they gave it half-heartedly, at irregular intervals in insufficient dosage and without due regard to the possible early complications by other infecting organisms. In considering the benefits from vaccines in acute urethritis the essential factor is to obtain an early and complete cure.

It is well known that the development of chronic gonorrhea depends, to what extent deep-seated involvements take place during the acute or subacute stages of the infection. When the gonococcus invades the deeper structures of the urethral mucous membrane and its resulting destruction, a stricture is the natural consequence. Involvement of the prostate, seminal vesicle or epididymitis necessarily places the infection beyond effective antiseptic local treatment. A swollen urethral mucous membrane with a possible abscess formation is certainly not conductive to adequate drainage to prevent upward extension of the infection with its resulting complications. The only condition that makes such deep-seated infections by the gonococcus possible is insufficient systemic resistance to the gonococcus. That gonococcus vaccine has a marked influence in developing rapid systemic resistance to the gonococcus is well illustrated when used in adequate dosage in the early stages of urethritis. Invariably it will be found that the burning sensation with pain when urinating will be relieved within 24 to 30 hours. Where an adenitis exists the swollen condition of the glands will subside at the same time. The advice to urinate often and thereby gain the advantage of frequently flushing out the urethra is more readily heeded when it is not a painful procedure than where the urine must pass through a sensitive swollen urethra. In some cases the discharge becomes much less within a few days and by repeating the inoculations regularly at three or four-day intervals a complete cure takes place within three or four weeks without any other treatment. In others the discharge becomes more profuse, but it is invariably much thinner, containing cells showing active phagocytosis and much serum and in this way also facilitates drainage. Where the discharge shows a tendency to persist, appropriate local treatment should be instituted to get rid of the surface infection.

Stock gonococcus vaccine is usually employed, it having been found that autogenous preparations are of no special

advantage. The early advent of staphylococcus complications should not be overlooked. Staphylococci are present in the normal urethra and soon after the gonococcus sets up an irritation the staphylococci present also begin to multiply and become a part of the pathological process. For this reason I have found it of advantage to employ a staphylococcus in conjunction with the gonococcus as soon as treatment is started. Many physicians preferably employ a mixed vaccine containing in addition to the gonococcus and staphylococcus also the other pyogenic organisms, streptococci, pneumococci, and colon bacilli, which are common complicating factors in chronic gonorrhea.

From experience we find that gonococcus vaccine has heretofore been used in entirely too small doses to obtain the best results. In the chapter on dosage I pointed out that therapeutic immunizing responses may be obtained from many different sized doses, inside of certain limits. In the use of gonococcus vaccine it appears that the prevailing dosage ranged along the minimum margin line of effective doses, consequently many good results were secured, but with enough failures to become at times discouraging. I know of reliable physicians who start treatment with 0.2 c.c. of a gonococcus vaccine containing 1,000,000,000 gonococci per c.c., in conjunction with other pyogenic organisms, who claim excellent results. This would give the patient a 200,000,000 dose with which treatment is started. The dose is then gradually increased to 1 c.c., making inoculations at three to five-day intervals, depending entirely on reactions and the progress of the patient as a guide for dosage. As a rule the dose may be increased to one cubic centimeter within four or five inoculations. It is found that reactions are not really severe and are of short duration. I have treated two cases with this large dose method and must say that the patients did well. Dr. Carl Muenz, of Detroit, who has used vaccines exten-

sively, tells that he uses a combined stock vaccine containing gonococcus 1,000,000,000, streptococcus 100,000,000, pneumococcus 100,000,000, colon bacillus 200,000,000, pseudo-diphtheria bacillus 300,000,000, and staphylococcus albus 800,000,000 per c.c. in his acute cases of urethritis with excellent results. He gives 0.5 c.c. for the first dose and repeats the same dose the next day. He usually finds an increased amount of discharge for the first three or four days, but it is very thin, containing much serum. After that inoculations are made at four or five-day intervals, gradually increasing the dose to 1 c.c. No local treatment is employed. Methylene-blue tablets are given in conjunction with the vaccine. In the seven successive cases thus treated he finds a complete cessation of symptoms inside of two to four weeks.

It has been found that reactions from a vaccine are less severe, producing less malaise when a laxative is used in conjunction with the vaccine. Dr. G. A. Persson, of Mt. Clemens, (Bacterial Therapist, July, 1915) is very insistent in his contentions to this effect. He prefers the hypertonic mineral waters for this purpose. Some doctors give a dose of calomel. Where these large doses of vaccine are given, I think it is of distinct advantage to employ a suitable laxative in conjunction with the vaccines.

While early vaccine treatment—and the earlier the better—is of great importance to obtain the best ultimate results, it is of even greater importance to continue treatment for a sufficient period of time to completely extinguish every focus of a dormant infection. The average patient is too much inclined to neglect treatment when clinically there is no indication of trouble. Treatment should be continued for at least a month or more, making inoculations at weekly intervals with the ultimate large doses of 1,000,000,000 organisms, after all symptoms of the disease have

subsided. In this way sufficient immunity can be built up to get entirely rid of the infection.

The distinct advantages from using gonococcus vaccine early in the course of an acute gonorrheal infection are: more comfort to the patient, more complete cures in a shorter space of time, fewer cases of epididymitis, and iritis, and cases developing into arthritis are practically eliminated.

CHRONIC GONORRHEA.

The great prevalence of chronic gonorrhea is sufficient evidence that prevailing methods of treatment in acute cases are not efficient.

The opinion, however, as to the value of vaccines in this treatment of chronic gonorrheal affections is practically unanimous in its favor. One characteristic of gonococcus infection is that this organism prepares the field for the growth of other organisms which in time often crowd out the gonococcus entirely or make this organism a secondary factor in the infective process. So, in considering treatment by active immunization with vaccines, the role played by the secondary invaders must receive careful attention. Of these the staphylococcus, streptococcus, pneumococcus, colon bacillus, and pseudo-diphtheria bacillus are the most common and most constant. All of these organisms may flourish side by side in an infection and they all have a tendency to cause chronic localized infections. From this it can readily be seen that where deeper structures—beyond the reach of local treatment—become involved, the building up of a resistance to overcome the infecting organisms offers the only hope of effecting a cure. That bacterial vaccine inoculation is the best means at our command towards this end is now generally admitted.

Stock vaccines containing in addition to the gonococcus the other commonly found organisms are now most extensively employed, although there are some physicians who

still prepare autogenous vaccines from the organisms found and add some stock gonococcus suspension. My experience has led me to believe that no advantage is gained from the use of autogenous vaccines in these cases except when unusual organisms are found.

Much discussion has developed as to the proper sized dose with which to start treatment and to what extent the dose may be increased. As a whole, much larger doses are being employed than was customary a few years ago. We find that more extensive infiltration at the point of inoculation, and more reaction develops from vaccine inoculations in these than in acute cases, and for this reason treatment should be started with somewhat smaller doses. As a routine, 0.1 c.c. of a combined stock vaccine containing gonococcus 1,000,000,000, streptococcus 100,000,000, pneumococcus 100,000,000, colon bacillus 200,000,000, pseudo-diphtheria bacillus 300,000,000, and staphylococcus 800,000,000 per c.c. may be given as an initial dose. If not much reaction develops the dose may be rapidly increased to 1 c.c., making inoculations at three to five-day intervals. If marked reactions should take place the dose should not be increased until there is but little reaction and inoculations should be made five to seven days apart. As a rule it will not be necessary to increase the dose beyond 1.0 c.c., but in some cases it is found necessary to work the dose up to 2.0 c.c. Where bacterial examinations show other organisms present corresponding stock vaccines or an autogenous vaccine should be employed.

A most important factor in the treatment of chronic gonorrhea with vaccines is persistence. The patient should always be told that it is impossible to know how long it will be necessary to continue the treatment. In many cases the immunity builds up slowly where crowding the treatment will not be tolerated. When a stricture is present, proper surgical treatment is necessary, and it is found that

operations for strictures are more successful when combined with vaccine inoculations. Local treatment to take care of surface infections is also of great importance.

Dr. G. A. Persson (Bacterial Therapist, March, 1915) devised a system of local treatment for chronic urethritis which combines the principle of drainage with the local application and germicidal influence of the lactic acid bacillus. It consists of cords saturated with lactic acid bacilli and their enzymes which are then dried and coated with cocoa butter so they may be readily inserted. The cord is allowed to remain in the urethra until it is necessary to urinate, usually four to six hours. One daily application is advised, although in some cases it may be employed twice daily to advantage. He sums up his results as follows:

"Total number of cases, 164.
"Duration of infection, from 90 days to 20 years.
"Duration of treatment, from 14 days to 94 days.
"Number of cases cured at the end of treatment, 126.
"Number of cases improved, 19.
"Number of cases unimproved, 7.
"Number of cases not completed, 10.

"Only such cases were considered cured in which not only clinical symptoms were absent, but repeated bacterial examinations proved negative."

In prostatic cases gentle massage of the prostate to evacuate pus accumulations is necessary so immunizing substances may reach the germs and finally eliminate them. It cannot be expected that antibodies in sufficient quantities to kill the germs will find their way into the depths of pus accumulations. Vaccine treatment should be persistently followed up with steadily increasing doses, often for six months or a year. As long as shreds are found in the urine we should be suspicious that the gonococcus has not been eradicated and only by negative findings on repeated bacterial examinations of the shreads by culture and micro-

scopic methods should such a case be considered free from gonorrhea.

To gauge the dose of a gonococcus vaccine when used in conjunction with other organisms I have found it convenient to employ a gonococcus suspension of 1,000,000,000 organisms per c.c. and a mixed vaccine containing the other organisms in proper proportions. By taking the desired amount of each vaccine the dose may be conveniently controlled.

Every patient should be informed of the importance of continuing treatment at one or two weeks intervals for six weeks or two months after all symptoms of the disease have left. Any immunity that has been built up to the gonococcus is liable to soon wear off and if the gonococci are not all killed a relapse is liable to follow. By continuing the treatment the immunity may be maintained long enough to finally eradicate the germ.

EPIDIDYMITIS AND ORCHITIS.

Some of my early experiences in the use of bacterins were in cases of epididymitis and the observation as to the good results then obtained have been confirmed many times since. I well remember one of these early cases. The patient was a young man living at home in a good family. He had been under the care of a good regular physician who treated him for the gonorrhea according to conventional methods, but after having suffered for nearly two days from an epididymitis, called me to take charge of the case. He was extremely fearful that his folks would find out what the trouble was, and if his suffering must continue much longer there was no way of escaping it. Hot fomentations, ice bags, and other methods of local treatment are inconvenient and are liable to arouse suspicion among members of the family. A dose of gonococcus vaccine was given at once. Twelve hours later the pain began to let up and in twenty-four hours he felt quite comfortable, no local

treatment of any kind having been employed. The vaccine treatment was continued and in a week's time the swelling was practically gone, and eventually the gonorrheal infection was entirely eliminated under the vaccine treatment. We succeeded in effecting a cure without incurring the distrust of the immediate relatives. I never saw a more grateful class of patients than young men who were relieved from an epididymitis or orchitis without arousing suspicion as to the nature of the trouble, and with the use of gonococcus vaccine this can be done.

The opinion as expressed in current medical literature by vaccine users is practically unanimous in favor of employing gonococcus vaccine in the treatment of epididymitis and orchitis. Early treatment is very important to obtain the best ultimate results. Intense prolonged inflammation with pus formation has a tendency to destroy the function of the epididymitis. Vaccines can not restore destroyed tissues. With the early application of gonococcus vaccine the inflammation will be held sufficiently in check to avoid destructive inflammatory developments and instead of leaving the patient with an indurated epididymis the organ is again restored to its former condition.

These acute cases, especially in the presence of fever, tolerate vaccine inoculations well and should receive sufficiently large doses at comparatively short intervals. From 100,000,000 to 200,000,000 may be given as an initial dose and if no material reactions develop the same dose may be repeated the next day. Gradually increasing doses should then be given at two to four-day intervals, increasing the dose to 1,000,000,000 within four or five more inoculations. Where marked reactions follow injections the dose should not be so rapidly increased and inoculations made at longer intervals.

The staphylococcus being an early complicating factor in gonorrheal infections, it is good practice to include a

stock staphylococcus suspension in suitable dosage with the gonococcus vaccine and where an epididymitis or orchitis develops after a chronic gonorrhea the other pyogenic organisms usually found in such cases should also be included in the vaccine.

NON-GONORRHEAL ORCHITIS.

Several cases of orchitis have come under my care where there was no evidence of gonorrheal infection. One case was in a man on whom a doctor had passed a sound several days before. One testicle was badly swollen and very tender. The inflammation was acute and had developed within two days. The acute character of the infection ruled out tuberculosis. The man assured me that he had never had gonorrhea and the fact that he was married and had raised a family of seven children was good evidence of his contention. He was promptly relieved with streptococcus-staphylococcus combined vaccine. Two other cases of orchitis in which no evidence of a gonococcus infection existed were treated with the same vaccine with equally gratifying results.

Orchitis being a common complication of mumps and more recent investigations having demonstrated that mumps are caused by a certain strain of streptococcus, it has occurred to me that possibly the two last cases referred to may have had parotiditis with a slight involvement of the parotid gland, but more severe lesions in the testicle. I have on several occasions heard from doctors who claim to get good results from stock streptococcus vaccine in the treatment of this disease, which would also account for the benefits derived in the two cases referred to.

ENLARGED PROSTATES.

From the constant presence of colon bacilli and other pyogenic organisms in enlarged prostates and from the close relationship between infections and tissue proliferation there can be no doubt but that these infecting organisms

are the etiologic factors in enlarged prostates. From this viewpoint vaccine inoculations certainly should be of benefit. The surgical treatment of enlarged prostates while beneficial is not what it should be. If these cases can be brought under control with the use of vaccines, especially when applied in the early stages of the trouble, much will be gained. Several of my acquaintances in the profession are employing vaccines in this capacity and they are claiming good results. A combined vaccine containing colon bacilli, streptococci, pneumococci, and staphylococci would be indicated.

GONORRHEA IN WOMEN.

Infective inflammatory conditions of the womb, its adnexa and the pelvic tissues are, according to leading authorities, caused by the gonococcus in fully 75 per cent of known cases.

Staphylococci, streptococci, colon bacilli and other organisms are also found frequently. More often we have mixed infections of two or more of these germs. In the absence of a definite history of gonorrheal infection it is often difficult to make a diagnosis.

Gonorrhea in woman usually assumes a subacute form even in the early stages, often causing so little distress from the urethral infection that it is entirely disregarded and no disturbance will be observed until the infection has extended into the uterus with the inevitable leucorrhea. During this stage there is seldom much constitutional disturbance and not enough inflammatory action to cause much pain in the pelvic regions. Bacterial examination is of great aid in making a diagnosis, but a negative result is not conclusive, because gonococci may no longer be present in the discharge although the infection may be rapidly extending into the Fallopian tubes. After the infection has reached the Fallopian tubes there is more inflammation and

pain, often associated with considerable constitutional disturbance and fever. During this time there usually is pus formation and, in cases where the inflammatory process seals up the opening, the pus accumulates in the tubes.

Operative interference in the early acute stages is now generally regarded as not advisable on account of the danger involved and because many of these cases recover spontaneously and thereby save important organs that would otherwise be sacrificed. It is found that in from four to six months the pus in these tubes usually becomes sterile when operative methods may be employed without much danger of extending the infection.

From this brief consideration of the usual course of a gonorrheal infection in women, it will be seen that the progress is comparatively slow and not associated with a great amount of inflammatory activity. This is of diagnostic value because it is in sharp contrast to streptococcus or colon bacillus infections of the pelvic organs where rapid development of the inflammatory process, associated with much pain, swelling, fever, and constitutional disturbance, is the rule. A staphylococcus infection does not cause much pronounced disturbance and in gonorrheal cases is usually found associated with the diplococcus of Neisser.

The gonococcus is an organism that confines its operations largely to the mucous membranes, and being a surface infection it does not produce sufficient impression to adequately stimulate the immunizing mechanism. After the infection has extended into the Fallopian tubes, more constitutional disturbance is created and a gradual development of an immunity ensues with an occasional subsequent spontaneous recovery. The difficulty with this procedure, however, is that often the infective process does so much harm before an immunity is established that permanent injury follows.

By using a vaccine the immunizing mechanism may be

stimulated into activity during the early stages of the disease, thereby either aborting the infective process or so modifying it that no serious harm is done.

In successfully handling these cases the appreciation of mixed infections is a very important factor. Staphylococci are most frequently associated with gonorrheal infections and where not present they are liable to become a complicating factor at any time. Streptococci, colon bacilli, pneumococci, and psuedo-diphtheria bacilli are also liable to be present. Not infrequently other organisms may also be found. In these cases the more common pyogenic organisms often, during an acute infection and later on in course of time, entirely displace and eliminate the gonococcus.

The following case is an apt illustration:

This was a young woman whose husband had contracted gonorrhea about six months before they were married. About one and a half years after marriage I was called to treat her for an inflammatory condition in the region of the left ovary. She had been treated for some months by another physician, but steadily got worse. She was a highly educated, intelligent woman, had heard of vaccine therapy, wished to have it tried, and the attending physician insisted that I take charge of the case. Examination revealed a hard, extremely tender swelling to the left of the uterus, about the size of a small orange, and extensive tenderness on the right side as well. She was menstruating, but there was considerable pus mixed with the blood. Her temperature was 102½. She felt restless and suffered intensely, not having slept the previous night, although opiates had been given. Not much hope was entertained that any permanent result could be obtained without an operation, but vaccine treatment was resorted to with the expectation of relieving the acute symptoms before an operation would be undertaken. No bacterial examination of the purulent discharge was made because the findings

would have been unreliable, the pus being extensively mixed with blood from the menstrual flow. The acute inflammatory condition indicated that the gonococcus was no important factor, but that the streptococcus alone, or with some other common pyogenic organisms was responsible for the existing inflammation. Accordingly, a mixed streptococcus, pneumococcus, staphylococcus, colon bacillus vaccine was given. The next morning her temperature was down to 100, and pain much less, with the swelling subsiding. A day later another dose of the same vaccine was given. The patient rapidly improved, and after receiving six inoculations inside of five weeks' treatment, she made clinically a complete recovery. After three years she is still entirely well.

Early treatment with vaccines is just as important in cases of gonorrhea in women as in men and because of the fact that extensive mixed infections are more liable to take place early in the course of the infection than in men it is of decided advantage to employ, at once, a mixed vaccine containing the usual complicating organisms in addition to the gonococcus. The matter of dosage is also important. Entirely too small doses have been employed to get the best results. The initial dose of gonococcus vaccine should be not less than 100,000,000. If not much reaction follows an injection the dose should be rapidly increased within four to six inoculations to 1,000,000,000. Where considerable reaction follows inoculations the dose should not be increased so rapidly. Inoculations are preferably made at three to five-day intervals. A vaccine containing staphylococci, streptococci, pneumococci, pseudodiphtheria, and colon bacilli, should be given in conjunction with the gonococcus vaccine in the usual dosage for the purpose of controlling secondary invasions by these organisms. I am confident that many of the indifferent results heretofore attained were due either to insufficient dosage, a disregard of complicating infection, using the vaccine too

late, or a combination of these elements. My observations lead me to believe that when the vaccine treatment is started early and persistently followed up, but few women will require surgical treatment. If the infection has extended to the Fallopian tubes the patient should remain in bed until the inflammation has subsided. Drainage of a pyosalpinx through the womb may be maintained in most instances through the immunizing influence of the vaccine, in that it will prevent closing up of the tubes by swelling.

In the treatment of gonococcic infections in women, cognizance should be taken of the fact that almost invariably the ducts of Skene, or Skene's glands, as they are sometimes called, are almost invariably foci of infection but usually overlooked. Special stress must be laid upon the importance of opening up these ducts in order that the pent-up pus may be let out.

Where intense inflammatory conditions develop, associated with excessive fever and other constitutional symptoms indicating toxemia, it is almost certain that a streptococcus or colon bacillus infection has taken place and corresponding vaccines should then be mainly relied upon.

To emphasize my own contentions I will quote an interesting case report from an article by Joseph J. Boehm (Therapeutic Gazette, Jan. 15, 1912, p. 21) on the use of a mixed gonococcus-staphylococcus vaccine in treating gonorrheal infections. He says:

"All cases of prostatic gonorrhea, and gonorrheal arthritis, as well as epididymitis and orchitis, should receive the benefit of the combined vaccine. In February, 1911, the following case of interest was successfully treated with vaccine, and is a type of similar cases treated by me:

"Mrs. Z., aged 30, married. Three days after coitus her husband brought her to me for examination. He had been treated one week previously by me for urethral gonorrhea, contracted extramaritally. Examination of his wife showed a thick urethral and vaginal purulent discharge with gono-

cocci abundant in the urethra. One day afterward both her knee joints were tender; the left joint especially was so painful and swollen that she could not stand on the limb. I sent her to the hospital immediately. She showed signs of systemic gonorrhea within 24 hours after I had first seen her. There was a loud systolic murmur at the apex of the heart, the pulse was rapid, temperature 102 degrees F., face flushed and anxious looking, and the patient in great distress. The limb was immobilized on a splint, and local applications made as placebos. Cultures of the blood showed the gonococcus present in the circulation. The temperature in the first week went to 104 degrees. The patient was very sick, and on account of her endocarditis a probable fatal prognosis was given. She was placed from the beginning of her arthritis on mixed vaccine, given at intervals of three days. She received twelve injections, and at the end of that time her temperature dropped to normal and all signs of her systemic infection disappeared, except her cachexia, which followed her high temperature. The left knee-joint was swollen for three weeks, but as the fluctuation in it progressively diminished the joint was not aspirated. She was kept in the hospital for four weeks, and was then taken charge of by an orthopedic surgeon, who kept her in a plaster cast for several weeks. Outside of some ankylosis of her knee-joint she made an uneventful recovery."

Here again is a case of a malignant systemic infection responding to combined vaccine.

VULVOVAGINITIS IN CHILDREN.

Gonococcus vaccine is being successfully employed in vulvovaginitis in children. In these cases, as in other gonorrheal infections, the complicating infecting organisms is important.

B. Wallis Hamilton (Journal A. M. A., April 9, 1910, p. 1198), after an extensive use of stock vaccines in vulvovaginitis in children, concludes that: "Vaccine therapy has a place in the treatment of this infection in little children, for the following reasons:

"1. The short time required for a cure in over 85 per cent of cases.

"2. The ease of administration of the vaccine, no special apparatus or knowledge of technic being necessary.

"3. The vaccine is apparently harmless when used under aseptic precautions.

"4. It is not necessary to take the opsonic index, with its complicated technic.

"5. It eliminates irrigations, which direct the child's attention to its genitals, at times encouraging precocious masturbation. The frequent douches necessary in the irrigation treatment will, with the best of care and gentleness, produce some injury when continued over a long period of time."

CHAPTER XVI.

PUERPERAL SEPSIS AND INFECTIONS INCIDENTAL TO MATERNITY.

Puerperal Infections.

Fever a few days after a confinement is always regarded with apprehension, because it may be the first indication of the development of a dangerous infective process. While it is true that we often have in these cases a rise of temperature which subsides spontaneously in a few days, it is just the false hope that nothing serious will happen that is often responsible for costly delay in instituting proper treatment.

From an anatomical standpoint one could hardly imagine a more favorable condition for the development of a serious infection than the womb presents after a confinement. A large, blood-filled organ, with an extensive excoriated area from the previous placental attachment, it has much tissue and surface available for germ development, and the fact that the organ is undergoing subinvolution resulting in a lowered vitality also favors the infective process. The irregular inner surface of the womb with its many folds is an ideal incubator in which the infecting organisms may flourish, and being located in the abdominal cavity, the infection may readily extend to the peritoneum, with a resulting general peritonitis.

In some cases the infective process develops much more rapidly than in others, depending on the relative resistance of the patient and the virulence of the invading organism. To decide just when the local infection has turned into a general infection is practically impossible.

Local treatment, with the object of destroying the infection, is at best difficult to carry out, because the entire surface of the uterine cavity cannot be reached. Curetting, unless very carefully done, will do more harm than good

by exposing new surfaces for infection and by unavoidably manipulating an inflamed organ. If the infection has extended into the uterine tissue it cannot be reached by any local treatment. On this question Professor J. H. Carstens says (Journal A. M. A., Aug. 6, 1910, p. 476):

"By local treatment more harm is often done than good. Douches given by ignorant persons often implant new and virulent micro-organisms within the genital tract, while scraping and curetting and injuring the delicate mucous membrane opens new channels for absorption.

"When a localized abscess is formed which can be opened into the cul-de-sac of Douglas or somewhere else, I certainly believe it should be promptly opened; but as we see the disease generally several days after its onset, I think no local treatment will be of any avail.

"I have been all the more desirous of bringing this view before our section since reading the proceedings of the last German Association of Obstetricians, where Winter, in an exhaustive article, shows this most clearly, coming to the conclusion that simple absorption ceases as soon as the necrotic tissue is cast off; that simple local infection and endometritis stop soon without any treatment; that no local treatment will prevent deep or general infection, and that when absorption takes place and there are remnants of tissue still in the uterus, one should be tardy about removing them, as these are generally quickly cast off and the patient gets along just as well as with the most vigorous treatment."

From these considerations it should be evident that, unless the systemic resistance is sufficient to prevent spreading of the infection the case is almost hopeless.

In puerperal sepsis the streptococcus is by all odds the most dangerous micro-organism to deal with. The colon bacillus, the pneumococcus and the staphylococcus are also frequently present, either as primary invaders or as complicating factors in a mixed infection. Where there is a gonorrheal infection, other organisms are also liable to be

present. Extensive investigations have been made to determine whether in puerperal sepsis the streptococcus is introduced into the genital tract during confinement or if the infection possibly develops from streptococci present in the vagine before the confinement. From these researches it is quite clear that most cases of streptococcus infection are due to external sources, with occasional auto-infections. It appears that about 20 per cent of pregnant women at the time of confinement have streptococci in the vagina, but as a rule these streptococci possess a low virulence for the patient. When a gonorrheal infection is present, however, the more virulent types of streptococci are also liable to be present. Microscopic examination of slides prepared from the lochia are unsatisfactory as a means of making a bacterial diagnosis, because the non-virulent types of streptococci so often found in these cases are indistinguishable from the virulent ones. Hemolytic tests by cultural growths may throw some light on the subject, but some non-hemolytic types of streptococci are very virulent to certain individuals. The streptococcus is an unstable organism and under suitable cultural conditions the non-hemolytic varieties may be converted into hemolytic streptococci and vice versa. A non-hemolytic streptococcus present in the vagina before a confinement lives under cultural conditions entirely different from those after a delivery. A lacerated cervix with ragged and crushed tissues may be a soil sufficiently favorable to change a moderately virulent streptococcus into a virulent organism. In making cultures from the uterine discharge the variety of organisms often present makes reculturing necessary to identify the organisms. To procure a culture, a sterile curved glass tube should be passed up to the uterine fundus and the culture procured by means of a sterile flexible swab through the tube. Such a procedure, however, is always surrounded with the danger of carrying virulent organisms into the womb.

A blood culture is always the safest and most reliable method. By withdrawing some blood from a vein with a sterile syringe under aseptic precautions, cultures can be made on ascitic agar slants and in peptone beef tea, which can readily be examined after 24 hours' incubation.

Clinical symptoms often give some hints as to the character of the infection. Lea, in his excellent work "Puerperal Infection," p. 186, points out that:

"In streptococcic infection the discharge is often profuse and haemorrhagic, and soon becomes purulent; but there is no foetor. In the more severe types, the lochia may be scanty or cease entirely.

"In staphylococcic infection the lochial secretion is often profuse and purulent.

"The bacillus coli communis infection is attended by an offensive feculent-smelling discharge."

Lea (p. 146) considers a temperature of 100.4 inside of ten days after a confinement, with few exceptions, as due to an infection and that in slight infections the fever rarely goes beyond 101 degrees. Where the temperature reaches 103 or 104 within three to five days he considers the infection to be a more severe type, and the association of rigors often indicates that the organism has entered the bloodstream.

In the treatment of these cases therapeutic immunization with vaccines should never be postponed for the purpose of making a bacterial diagnosis. The streptococcus being the dangerous infecting organism, a dose of streptococcus vaccine should be given, and in sufficient dosage.

Beckwith Whitehouse, in a paper read before the Birmingham Branch of the British Medical Association, March 16, 1911, referred to the early use of vaccines in these terms: "To obtain the very best results it is most essential to attack the disease at the earliest opportunity. Too often valuable time is lost at the commencement of infection, time that can never be regained; and when at last vaccines

are employed they are but doomed to failure. To be of service a vaccine must be administered at the first possible moment, and before the micro-organisms have multiplied to any great extent in the blood stream. During the last twelve months in hospital and private practice I have treated twelve cases of severe puerperal infection by the vaccine method, and the importance of early treatment has impressed me much. Nine of the patients recovered and three died. Of the latter, two came under observation only on the day before death occurred, and a vaccine was employed simply as a last resource. The third patient received her first dose of vaccine on the seventh day of the disease, and although a well-marked reaction followed each dose, active immunization failed to check a severe attack of pneumonia, which proved fatal on the twelfth day after treatment. Of the cases that recovered, success was most marked in those patients to whom access was obtained at the commencement of the attack."

These puerperal cases give us some of the most beautiful illustrations as to what can be accomplished in the early stages of dangerous acute infections with bacterial vaccines. Time and again patients are seen in whom the fever and other symptoms indicate the development of serious trouble which clears up like magic after one or two inoculations. This may be regarded by some as simply an expression of over-enthusiasm, since it is known that many cases of simple postpartum infection recover spontaneously without any special treatment. Even after allowing for all such cases there is no room left for doubt as to the tremendous advantage of this method of treatment. During 28 years of active city practice I have had ample opportunity of observing the course of puerperal infections before and after using the vaccine. During the past nine years my experience in the use of vaccines for puerperal infections has been extensive. Here in Detroit where I have been supplying many physicians with bacterial vaccines, hundreds of cases have been treated under my directions, as a rule by telephone consulation and occasionally

the patient was seen in consultation. When a doctor inquired about treating a case I always had him keep me informed by telephone as to the progress of the patient. At first I recommended streptococcus or streptococcus-staphylococcus combined vaccine, but in later years I generally advised, especially where the temperature was high, the administration at once of 1 c.c. of a vaccine containing streptococcus 100,000,000, pneumococcus 100,000,000, staphylococcus aureus, albus and citreus each 200,000,000, and colon bacillus 200,000,000. This may look to a timid man like a dangerously large dose for a patient with a temperature of 105 and a rapid pulse, but it is surprising what little subjective reaction such a dose will develop in a severe toxic infection. Unless the patient is moribund, a drop in temperature of two or three degrees may confidently be expected within 24 hours. The same vaccine is usually repeated the next day. In all my experience there have been but three deaths, and a brief description of them will be of interest: The first case was of six weeks' standing. The woman was thin and very pale. There was no localized infection in any part of the body. A blood culture was taken by withdrawing some blood from a vein. Streptococci were isolated and an autogenous vaccine made. She died four days after the first inoculation. The second case was very acute. Four days after the confinement she developed a very high fever. I was called in consulation. She was unconscious, not even being aware that blood was taken from her vein. A dose of mixed stock vaccine was given, with some improvement the next day, but she died a day later; cultures from the blood showed gonococci. The third fatal case was that of one of our prominent general practitioners. He had previously saved a bad case with mixed stock vaccine—one that had been under the care of a midwife, had a high temperature when it came under his care, with delirium imminent. When this patient had improved, he mentioned to me another case of over a

week's standing and already delirious. This patient also received, at my suggestion, a mixed stock vaccine, and made some improvement for several days, but then relapsed. Anti-streptococcus serum was thereupon resorted to; but meanwhile an abscess developed back of the eyeball. The infection extended to the meninges, and she finally died of meningitis.

From observation of cases that came under my care, cases that were seen in consultation and the extensive opportunities that my relations to the medical profession offered for obtaining information, there can be no reasonable doubt as to the inestimable therapeutic value of vaccines employed early in the treatment of puerperal sepsis. It must be admitted that spontaneous recoveries often take place, especially where the infection is not severe, but why take chances? There is no way of knowing when a slight infection may become serious. I have found that this hope that the fever may pass off is the main cause why doctors do not employ specific immunizing measures early in their cases. Among the many doctors who have consulted me concerning these cases I rarely found that their patients had a temperature below 102. The impression that an autogenous vaccine is essential in a severe infection has persuaded doctors to request the preparation of autogenous vaccines. To illustrate: A doctor inquired by telephone how soon I could prepare an autogenous vaccine. On inquiry it was found that this was a case of abortion of three days' standing, with a temperature of 106.5. I advised a mixed vaccine at once and directed the procuring of a culture. The sending of the culture was neglected by the doctor, but the next day he reported a temperature of 102. The vaccine was given at daily intervals for three days and later at three to five-day intervals, with a complete recovery in two weeks. Where spontaneous recovery takes place there is often a prolonged debilitated condition

before the normal vigor is restored. When the vaccines are used a characteristic promptness in the improvement is observed. This is not only the case with the milder forms of infection but the more serious cases as well.

Dr. McColl, of Detroit, consulted me with regard to a case that illustrates this very nicely. The patient was young, had had a very hard labor. There was a large child, breech presentation and difficult instrumental delivery. The doctor used all aseptic precautions as regards cleansing, and wore rubber gloves. On the fourth day the patient developed a temperature which continued to go up until on the tenth day it reached 105 degrees. There was much tenderness over the abdomen and much tenderness and swelling in the pelvic cavity. Bacterial examination by the Detroit Clinical Laboratory showed pneumococci and staphylococci. I supplied a vaccine which he gave to the patient at once. The next day the temperature had dropped to 101 and the patient felt much better. On the evening of the same day, however, the temperature rose again to 102.5. I advised giving a pneumococcus-streptococcus-staphylococcus combination, assuming that a streptococcus might be present which was not found in the examination. After this combined vaccine, of which she received two doses, the patient steadily improved and in less than a week she was sitting up in bed with temperature normal, pain in abdomen gone, and, considering the severity of the illness, feeling very well.

As experience in the treatment of puerperal sepsis increases I have been more and more impressed with the importance of early treatment; the advantages of employing a mixed vaccine containing the four principal infecting organisms, streptococci, pneumococci, staphylococci and colon bacilli; the use of large doses; and the necessity of making inoculations at daily or shorter intervals until the extreme acute symptoms have subsided. The dose of strep-

tococcus and pneumococcus should be from 50,000,000 to 100,000,000, staphylococcus and colon bacillus from 100,000,000 to 200,000,000. In the more severe cases with a high temperature the larger dose should be given and in the less severe cases the smaller dose. Reactions in these extremely acute infections are much less marked than where the infection is not severe. I am fully aware that most writers on vaccine therapy recommend small doses in severe cases and larger doses in the less severe infections, but my experience has been sufficiently extensive to convince me that the reverse is true.

An extensive blood invasion by the micro-organism is no contraindication to the use of vaccines. In fact, it is just in these cases, especially when the vaccine is employed before the patient is moribund, that some of the most striking results are secured. A drop in temperature to within one or two degrees of normal within 24 to 36 hours may be confidently looked for and by repeating inoculations at daily intervals for a few days a normal temperature with other improved conditions will soon be reached. Such results can not be expected, however, if the infection has been allowed to progress before vaccines are given; until a large focus of infection with pus formation has developed. In such cases surgical intervention to establish drainage should not be neglected.

On account of a prevalent theoretical conception that bacterial vaccines are contraindicated in extensive acute infections their application in the treatment of puerperal sepsis has unfortunately been neglected. No reports have ever been published, however, where it was shown that harm was done by their use and the concensus of opinion is that the results were always beneficial or indifferent. That indifferent results should have been obtained is perfectly apparent from the dosage and intervals between inoculations that were so frequently employed. Often only 5,000,000 to 10,000,000 organisms were given as a dose and inoculations made at three or four-day intervals. Further-

more, treatment was often instituted entirely too late to expect any results. Allen ("Vaccine Therapy," fourth edition, p. 268), from an extensive experience in the treatment of septicemia, contends that he has never lost a case.

Possible Gonorrheal Complications.—In cases of fever after a confinement the question of a possible gonorrheal infection should always be carefully considered and where a reasonable suspicion exists that such an infection is present a gonococcus suspension should be added to the vaccine. By this means the dangers of an extensive gonococcus infection may be avoided, while infections by other organisms are also being taken care of. In such cases doses of 200,000,000 gonococci should be employed.

Dr. A. T. Slotts (Illinois Medical Journal, July, 1911, p. 6) reports the following interesting case: "A young woman gave a history of no pelvic symptoms until about one year after her marriage, at which time a slight vaginal discharge and some tenderness was noticed. Six months after these symptoms first appeared she passed through a normal confinement and puerperium. On the fourteenth day she had a chill and went to bed, complaining of considerable discomfort in the pelvis. Two days later I found the cul-de-sac filled with fluid and the posterior vaginal wall bulging. A history of chronic gonorrhea in the husband, together with the information that the baby's eyes had been sore after birth, caused me to suspect gonorrheal infection. A culture from the vaginal and cervical secretions did not corroborate my suspicions. However, I did not give up the opinion that this was a gonococcus infection, and administered a fresh stock vaccine of this germ every fourth day. Her temperature reached normal on the thirteenth day after beginning treatment, the bulging cul-de-sac subsided and her recovery was rapid and complete. In all, five doses were given. One year has elapsed since her recovery, and she states that she has had excellent health and has no vaginal discharge or pelvic symptoms of any kind."

PROPHYLACTIC INOCULATION IN OBSTETRICAL PRACTICE.

The prophylactic use of vaccines in midwifery is of great importance, because there is always some danger of infecting the patient while making the necessary examinations and there is unquestionably some danger of infection from germs normally found in the genital tract. Many cases of virulent puerperal fever occur in cases where delivery was entirely normal and no examination had been made. From an extensive review of the literature on the bacterial investigations of the germs found in the vagina of pregnant women by A. W. W. Lea, in his most valuable book "Puerperal Infection," it would appear that streptococci are found in about 20 per cent of the cases. No doubt a large majority of these organisms are not virulent and exist in the vagina as saprophytes, but from microscopic examination and laboratory tests they cannot be differentiated from streptococci derived from a severe infective process. It is not at all unreasonable to suppose that in many cases these organisms become active and produce fevers of a mild type, while in exceptional conditions where the immunity of the patient is low they may cause a serious septicemia. Staphylococci, colon bacilli and other organisms are also frequently found.

We know that serious infections depend on two factors, the virulence of the organisms and the susceptibility of the individual. Thus organisms of low virulence may cause serious infections in very susceptible individuals, while more virulent organisms would cause but little or no trouble in non-susceptible persons. So in the last analysis immunity to these infecting organisms is an all-important factor.

Where there is so much opportunity for infection as presents itself in puerperal cases, the question of prophylactic immunization with bacterial vaccines naturally suggests itself. In most deliveries more or less laceration of

the cervix or perineum takes place, with the resulting opportunities for infection. Besides this one cannot overlook the inherent possibilities of the placental surface as an excellent culture medium for those germs which may chance to lodge there.

A good and perfect union of these lacerations after delivery is a very important factor in the completeness of the recovery after a confinement. It does not require much of an infection to prevent perfect union of lacerated tissues. Organisms of low virulence may suffice to do much mischief here. With the use of bacterial vaccines the body resistance to infecting organisms can be materially raised and midwifery presents a condition where the principal of prophylactic immunization should be taken advantage of.

Mrs. A. K. had been confined once before, at which time the perineum was lacerated into the rectum and neglected, so there was no union. Delivery in the second confinement was normal, but the small remnant of perineum was lacerated into the rectum, the tear extending nearly two inches upward. As the torn surface was small, I dissected away enough mucous membrane to make a proper perineum after stitching the parts together. The tear above the perineum was stitched with twenty-day catgut and the perineum was united with silkworm gut. For some reason the stitches made with the catgut gave way during the second day, leaving a rectovaginal fistula, through which the fecal matter passed freely into the vagina.

A more unfavorable condition for healing a lacerated perineum could hardly be imagined. I gave the patient colon bacillus and streptococcus combination vaccine from the start, making four inoculations at three-day intervals. There was no local treatment employed. There being almost a continual discharge, cleanliness was altogether impossible. Very little inflammation followed, resulting in a good union of the wound and sphincter muscle. The

stitches were removed on the thirteenth day, when there still existed a rectovaginal fistula. Two weeks later, however, to my surprise and gratification, the fistula had closed. This is an extreme case, but it aptly shows how these vaccines will prevent bacterial invasion by raising the systemic immunizing power.

Dr. H. L. Ulbrich, of Detroit, informs me that he has used combined streptococcus-staphylococcus vaccines in over one hundred cases of confinement as a prophylactor with entirely satisfactory results. He gives the vaccine not later than one day after the confinement. One case of postpartum hemorrhage deserves special mention. The necessity of removing blood-clots and breaking off adherent pieces of placenta made frequent insertion of the hand into the uterus necessary. A dose of vaccine was given and not the slightest fever or local infective disturbance developed. A week later another hemorrhage took place which required more intra-uterine manipulation with the additional risk of infection. A second dose of vaccine was given and an uninterrupted recovery without fever took place.

Dr. R. L. Pfeiffer, of Detroit, informs me that he has used the vaccines in this way, giving a dose in every case not later than a day after confinement. He says that he has had several cross presentations and other conditions which required much manipulation, but no infective trouble developed. He finds that cases receiving prophylactic doses of vaccine are more vigorous and do better generally than those not receiving vaccines. His experience with vaccines in the adjunct treatment of lacerated perinei shows that better and more prompt union takes place after stitching the parts than where no vaccine is used. In these cases he gives streptococcus-staphylococcus and colon bacillus vaccine. He is so favorably impressed with the prophylactic value of vaccines in midwifery that he would not confine a case without using them.

From what information may be obtained by a study of the literature on this subject and from my own observations, I am confident that we have no other means at our command that will so effectively avert dangers and unpleasant consequences in puerperal infections as the timely use of bacterial vaccines.

I cannot impress the fact too strongly that these means can be advantageously used as prophylactors as well as curative agents, and every physician would do well to have them on hand for immediate administration. They are not expensive, retain their potency for a long time, and are without the least iota of danger.

Streptococcus, staphylococcus and colon bacillus infections are so common that occasions for advantageously using these preparations are almost daily met with by the general practitioner.

MASTITIS.

Mastitis is one of the disagreeable and sometimes serious complications met with in obstetric practice. The mammary gland during the first week after confinement seems to be particularly susceptible to infections. This is probably due to an infecting organism lodging in some of the milk ducts and from there extending into the tissues. The most usual organism found in these cases is the staphylococcus, though streptococci are also found. When any portion of the gland becomes inflamed and feverish, it is a sufficient clinical indication that an infection is going on, and the necessity of using a vaccine is apparent. A dose of streptococcus-staphylococcus vaccine should be given at once to immunize against these organisms. This is being successfully done with very gratifying results.

PHLEBITIS.

Phlebitis is not uncommonly seen before and during confinements, especially in cases of varicose veins, and for this reason this ailment deserves mention here. The sta-

phylococcus or streptococcus are usually the infecting organisms, although other germs may also be present. Streptococcus-staphylococcus combination vaccine, when used in these cases, gives the best results. I have seen conditions after confinement, which from the extent of the veins involved promised to cause serious trouble, disappear after two injections of streptococcus-staphylococcus vaccine. One case occurred in a woman during the seventh month of gestation. The veins of one leg had for some time been varicosed and at this time became extensively inflamed. She was very much alarmed on account of a very tedious recovery from the same trouble on a previous occasion. I assured her that the vaccine method of treatment would avoid any serious complications and thus relieved her mental state. After two inoculations at five-day intervals the entire inflammatory process subsided and she went on to full term without further trouble. The same treatment should be equally applicable in other cases of phlebitis.

Dr. Huegli informs me that he has recently treated two cases of phlebitis with vaccines with most gratifying results.

Dr. H. J. Hoare (Bacterial Therapist, November, 1913) reports an interesting case as follows:

"On the 10th of August the patient was delivered of a normal child. No complications arising, the patient was dismissed on the tenth day after delivery seemingly in good health, and was seen again just two weeks after the birth of her child, and when questioned regarding her health said she was feeling fine. Two days later I was called, and found the patient in bed complaining of a pain, quite severe, in the right groin. Her temperature was about 100. I administered a cathartic, and used the enema, applied a 50-per-cent Ichthyol ointment down the course of the long saphenous vein, and elevated the legs. The following day (27th) I administered one-third contents of a 1 c.c. ampule containing streptococcus 100,000,000, pneumococcus 100,-

000,000, staphylococcus pyogenes aureus, albus and citreus each 200,000,000, colon bacillus 200,000,000. On the 30th of August I gave ½ c.c., September 3 I gave 1 c.c., and on the 8th of September I repeated this last dose. In all, I administered four doses of the vaccine. On the 9th of September my regular visits ceased. On the 2nd of October I again saw the patient, and was informed that she had walked quite a little distance the previous evening. She had been up to the table and about the house for some days previous.

"Now there may not be anything phenomenal about this, but when I say that the infection attacked the other leg, and in both of them extended the complete length of the vein, and that during the active process there was but very little swelling of the limbs, and after a few days practically no pain over the course of the veins, I believe I am justified in thinking that the disease ran an unusually light course. I attribute the almost entire lack of swelling and pain to the combating of the inflammatory process by the vaccine. I do this for the reason that I have seen all the other measures I employed carried out with scrupulous care by others but no vaccine given, and the patient suffer intensely from the swelling and the agony along the line of the vein, and at the expiration of three months not be able to walk any better than this particular patient does in six or seven weeks.

"I am not submitting the tedious record of temperature. In respect to this feature I did not notice any marked variation to the type which runs in this affection, but the temperature certainly stopped short before the time we are told it does.

"This report may not be of any value to others because I am not checked by an authority of national or international reputation, but it is fairly good evidence to me, and if I am so unfortunate in the future as to have another case of the kind, I certainly shall use the same treatment."

THROMBO-PHLEBITIS.

In thrombo-phlebitis we have a condition that usually develops from an infection of thrombi in the veins beneath the placental site, or from the pelvic veins which extend

from thence to the larger veins. This may readily produce an extensive thrombosis. Frequently small blood-clots in the pelvic veins soften and the broken-down substances enter the blood current, setting up a pyemia or septicemia. Staphylococcus, streptococcus or, at times, both organisms are usually found. This condition usually sets in during the second week of the puerperium, the infection, which is often of a mild character, gradually extending along the veins. If such an infection were aborted in this early stage by the use of vaccines, thrombo-phlebitis and its attendant pain and danger would be avoided. Where extensive thrombi develop the condition is always very serious. Here we have a condition of a general infection combined with the plugging of large veins which interferes with the proper circulation of the blood in the leg, favoring the formation of metastases. From the serious character of the infection a high mortality rate under conventional treatment should be expected. Lea ("Puerperal Infection," p. 178) places the average mortality at 60 per cent.

Dr. A. P. Ohlmacher, of Detroit, informs me that he has treated three severe cases of thrombo-phlebitis resulting from puerperal infections with autogenous vaccines which he prepared from the streptococci isolated from the patient's blood. They all made good recoveries. He also told of a case of thrombo-phlebitis occurring in a man during the relapsing stage of typhoid fever which he treated with vaccine. He isolated typhoid bacilli from the patient's blood from which he prepared the vaccine used in the case. This case was so far advanced that any method of treatment appeared hopeless, but improvement was observed in 24 hours after using the first dose of vaccine and he ultimately made a complete recovery.

Dr. A. G. Huegli, of Detroit, courteously gave me the following case report:

"On Dec. 1, 1911, I was called upon to treat Mrs. Otto

K., age 26, who three weeks previous to this had been instrumentally delivered of her second child. The accouchement, I am told, was tedious and difficult. However, no lacerations or uterine sepsis occurred. On the tenth day violent pains shooting down both lower limbs, chills, fever and a slight swelling of both thighs proved to be the onset of a thrombo-phlebitis of no small extent. The patient became very ill. Her attending physician summoned an expert consultant. Her condition grew steadily worse and her first physician was discharged. A homeopath was called, who later giving the relatives a hopeless prognosis, was also discharged.

"Two weeks after the onset of the phlebitis I found her in this condition: Extremely anemic, pulse 120, temperature 101, cough, expectoration, passive congestion of lungs, no cardiac lesions, slight tenderness over uterus, moderate swelling of both thighs, legs and feet. Exceedingly painful spots in calves, middle of thighs, and also over the left sacro-iliac fossa, where later an abscess developed and was drained. Cramps in the abdomen accompanied frequent diarrhoea.

"The following routine treatment consisted in giving at different periods as required, digitalis, strychnine arsenate, iron, pepsin, gentian, hydrochloric acid, opiates and laxatives. Both limbs were painted twice daily with a 20-per-cent Ichthyol solution and swathed in bandages.

"I attribute her complete recovery chiefly, however, to the use of stock vaccines which were administered early in my treatment. They consisted in a mixture of streptococcus 30,000,000 and staphylococcus 100,000,000, prepared by Dr. G. H. Sherman. Two such injections were given at an interval of four days. After each a slight exacerbation of all symptoms took place with temperature rise of two and three degrees and delirium. A most noticeable improvement soon followed and on the 31st of January, 1912, I discharged her from my care as recovered."

Dr. Huegli has since then treated one other case of thrombo-phlebitis and informs me that equally good results were obtained in this case.

These results are certainly a sharp contrast to those obtained under the operative and other forms of treatment.

ENDOMETRITIS.

Non-gonorrheal infections of the womb which take on a chronic character are common after a confinement or miscarriage. This is particularly true in the presence of a cervical laceration. Subacute or chronic infections are probably the principal cause for a subinvoluted uterus. The large, soggy uterine walls with a boggy mucus lining offers a good soil for the growth of pathogenic organisms. The usual pus-cocci, staphylococci, streptococci, pneumococci, and colon bacilli are most constantly found. Other organisms, both pathogenic and non-pathogenic, are also found.

The importance of properly repairing a lacerated cervix to relieve chronic inflammatory conditions has been recognized for a long time. So, when we consider the use of vaccines in the treatment of chronic uterine infections it must be remembered that they cannot take the place of surgical measures or replace a retroversion. But, where an infection exists, appropriate vaccines can always be employed to advantage.

In gynecological practice many infections are met with that are not primarily due to the gonococcus. Metritis, cervicitis and vaginitis are amenable to local treatment, but every practioner knows that there is a great tendency for the patient to relapse when local treatment is discontinued. Women will take local treatments faithfully for leucorrhea when there are prospects for a permanent cure, but so many women find that the leucorrhea returns after local treatment is discontinued that they become discouraged and abandon treatment entirely. If the infective character of these affections and the fact that localized infections of this character cannot be readily eliminated by local measures were more appreciated, less reliance would be

placed on this method of treatment. By combining local treatment with therapeutic immunization to build up a resistance to these germ invasions much more can be accomplished than when either local treatment or vaccines alone are relied upon. Furthermore, when an operation for a lacerated cervix or a currettement is necessary the problem of infection plays a most important part as to the ultimate result. Aseptic surgery may be carried out to the utmost degree, antiseptics may be employed to destroy the germs, but infecting organisms lodged in the deeper structures will not be eliminated and if the immunizing resistance of the patient is not up to par, extensions of the infection into the sewed tissues of a repaired laceration or the curretted surface may be expected. Before operations of this character are undertaken local treatment is usually practiced to bring the patient into condition for the operation. For this preliminary treatment vaccines corresponding to the infecting organisms present should be regularly employed in conjunction with local measures. As a rule a stock vaccine containing streptococcus, pneumococcus, staphylococcus and colon bacillus, given in the usual dosage, will answer every purpose.

Bail Hulies, F. R. C. S., Pathologist to the Royal Infirmary, Bradord, (British Medical Journal, June 14, 1913), in considering the use of vaccines in cases of leucorrhea, says:

"Any inflammatory condition in the uterine adnexa will by contraction tend to deviate the uterus and cause passive congestion with leucorrhea. Cultures taken from inside the cervix in these cases have shown mixed infections, the commonest form of organisms being the B. coli, a diplococcus, and staphylococci.

"The vaccine base should be given prior to rectifying the uterus, so as to raise the immunity. I have seen many cases made worse by curettings and other operative procedures performed when the patient's immunity was low, but I have never seen anything but good follow when the surgi-

cal procedures have followed the second inoculation of the vaccine."

Vaccine treatment should be continued for some time after a curettement. By this means the inflammatory condition will subside more rapidly and thus effect a complete recovery in less time.

Cervix lacerations with the resulting chronic irritation has long been recognized as an important predisposing cause of cancer. The importance of the accompanying infection as the primary factor in keeping up the irritation, to my mind, has not received enough attention. While no doubt much of the irritation following a laceration is due to the uterine mucous membrane coming in contact with the acid secretions of the vagina, yet such an irritation certainly creates a favorable condition for germ development and in the end chronic infection becomes the main irritating element. No doubt many of the failures to secure a good union in repairing a lacerated cervix with development of a subsequent cancer was due to infection. Furthermore, in some cases where union does take place a chronic infection continues in the scar tissues with a resulting cancer due in all probability to the irritating influence of the infection. If by the use of vaccines these chronic infections, with their resulting irritation, can be eliminated, much will be accomplished towards preventing uterine cancers.

Pelvic Cellulitis.

In the extensive acute infections of the pelvic organs, or pelvic cellulitis, the streptococcus is, in most instances, the important pathogenic agent with the colon bacillus and staphylococcus as complicating agents. In these cases, especially when the infection is associated with considerable fever, the same rule that applies to treating other extensive acute infections with vaccines also applies here. Early treatment is most important if abscess formation is

to be avoided. A polyvalent stock vaccine containing the usual infecting organism should be employed at once and given in comparatively large doses. Inoculations are repeated at daily intervals to advantage until the more acute symptoms and fever have subsided, when the intervals between inoculations may be extended to three or four days. Where an abscess has formed, drainage must be established. It will be found, however, that if vaccines are employed and an abscess does develop it will not be so extensive, and so large an amount of inflammatory infiltration with a rigid fixing of the uterus will not take place. I have seen cases of extensive pelvic cellulitis with a high temperature become fairly comfortable within one day after a vaccine inoculation and go on to recovery without abscess formation after a few more vaccine inoculations.

VOMITING DURING PREGNANCY.

Vomiting during pregnancy is one of those intractable ailments that often refuses to yield to medication and other treatments. John D. Seba (The Journal of the Missouri State Medical Association, January, 1916) contends that this vomiting is due to infection and finds that good results are obtained from the use of a mixed vaccine containing colon bacillus, streptococcus and staphylococcus, given in the usual dosage.

CHAPTER XVII.

WOUND INFECTIONS.

Vaccines in Wound Infections of Minor Surgery.

The successful handling of infected wounds is a very important factor in general practice. If we could have accurate statistics of the seemingly insignificant injuries in which deleterions consequences were caused by infections the showing, no doubt, would be appalling. Many a person has lost a limb or his life through such an infection that was not brought under control.

Abrasions of the skin from slight cuts, scratches, needle pricks, thorn pricks, trampling on a nail, etc., are of such common occurrence that ordinarily they are disregarded and heal without any special treatment; but not infrequently these trivial injuries become infected with virulent pathogenic organisms, and the patient consults the family physician only after trying various home remedies. Usually in such cases the infection has extended beyond the reach of local antiseptics, and the most important factor to prevent spread of the infection is constitutional resistance.

In cases of more extensive injuries a physician is generally called to take care of the fresh wound, but even in such cases, where the utmost care is taken in cleansing the wound with antiseptic solutions and dressings, infection sometimes takes place. Often wounds are penetrating or lacerated to such an extent that thorough cleansing to the point of an aseptic condition is impossible.

In treating wounds the possibility of a tetanus infection should always be kept in mind. This may be determined by the character of the wound and the circumstances surrounding the receipt of the injury. If the wound is superficial and has not been bandaged to exclude the air, a tetanus infection is not liable, because the germ, being anaerobic, will not grow when exposed to the air. The

tetanus bacillus is particularly prevalent in rich soil and barnyard manure, and deep wounds exposed to such filth should always be regarded as being in danger of a tetanus infection.

The tetanus bacillus causes very little, if any, local disturbance in a wound, and often, in a few days, disappears from the point of infection, while recent investigations tend to show that the tetanus toxin continues to remain in the nervous system.

Wounds caused by toy pistols in the hands of boys are particularly favorable to tetanus infections. The character of the dirt on the average boy's hand makes the presence of the tetanus bacillus always possible. The force of the explosion makes a small penetrating wound, carrying the dirt deep enough into the tissues to exclude the air, so that the tetanus bacillus can develop there. Since the germ causes no material disturbance, the injury is disregarded until constitutional symptoms develop. Wounds accompained by much local disturbance, inflammation, pain and swelling in the absence of tetanic symptoms can safely be regarded as not being due to tetanus infection.

In all cases where a possible tetanus infection is suspected antitetanic serum should be given without delay. The prophylactic value of this serum is well established, while its use as a curative agent, after the constitutional symptoms have developed, is not so pronounced.

After having excluded a possible tetanus infection, the question naturally arises as to what the infecting organism is. In many instances this can be determined by making a bacterial examination of the purulent matter discharging from the wound, but in most cases it is essential that treatment should be started at once to immunize the patient against the infecting organism and to prevent spread of the infection by the administration of vaccine, and to make

a bacterial examination usually means twenty-four hours' delay.

Delay in giving the vaccine is dangerous because, if the infection should extend rapidly, enough toxic material may be absorbed to paralyze the immunizing mechanism so that it can no longer be aroused into activity. For this very reason it is not advisable to use autogenous vaccines in the early acute stages. Nor should treatment be delayed to make a bacterial examination. The clinical symptoms in such cases are sufficiently clear to indicate what vaccine to use, until a bacterial examination can be made to verify the diagnosis if deemed necessary.

Furthermore, the wound is often of such a character that the infecting organism can not even be found. In the case of a penetrating wound made by trampling on a nail the germ causing the trouble may be carried deep into the foot, while the germs found at the point of entrance may be entirely different. In many cases where the skin abrasion was slight the original wound may have healed over, while the infection is progressing in the deeper tissues. In such cases a bacterial examination would also be impossible. The following cases are good illustrations:

A young man applied for treatment, having enlarged lymphatic glands above the elbow and in the armpit. Two glands above the elbow were as large as medium-sized hickory nuts, while the one in the armpit was not quite so large. They were very tender and had been noticed only three days. There was no red chain connecting them. The temperature was 99.5° F. Search for the source of infection showed a small scratch in the palm of the hand received five days previously; but it had healed over and a bacterial examination was impossible. By waiting until these glands suppurated a bacterial examination could have been made by procuring some of the pus, but that would have done the patient no good.

Upon consideration of the facts an approximate diagnosis was arrived at. The clinical symptoms indicated a streptococcus infection, but a staphylococcic infection was also likely as this organism is invariably present on the skin. Consequently a mixed vaccine consisting of 30,000,000 streptococcus pyogenes and 100,000,000 each of staphylococcus pyogenes aureus and albus was given. Improvement began within twenty-four hours after the inoculation and in five days the swelling in the glands had entirely disappeared. The recovery was complete without any further treatment.

No one can know what the consequences in this case might have been had the vaccine not been used. It was certainly better to head off the infecting process by giving vaccines than to have neglected it until an exact diagnosis could be made.

Take another instance: A man tramped on a nail. Forty-eight hours later, when I was called, the foot was badly swollen and very painful, but the inflammation was on the top of the foot and not where the nail had entered. The small opening was practically closed. His temperature was 100. Bacterial examination here would have been of no diagnostic value because the germs found at the point where the nail entered might not be the same as those causing the infection. Clinical symptoms indicated either staphylococcus, streptococcus or a mixture of both organisms. A mixed streptococcus and staphylococcus vaccine was accordingly given. In 24 hours his temperature was normal with the inflammation receding. Two days later another dose of the same vaccine was given. He made a prompt recovery and all signs of the trouble abated in a few days.

Nor should a case be considered too trivial to use the vaccine because small affairs are often very important to the individual concerned.

The following case is a good illustration: Miss G. H., a professional pianist, slightly pricked her middle finger at the root of the nail with a needle. Four or five days later her finger was considerably swollen and so painful that she was not able to use it. The following day she consulted me. Careful examination did not reveal pus. I gave her a dose of streptococcus-staphylococcus combination vaccine and advised hot water compresses as a local dressing. The next morning it was distinctly evident that there was pus under the root of the nail, the lunula appearing yellow. A small cut through the nail at this point established drainage and, for the location, considerable pus was discharged. The pain and inflammation subsided almost at once. The pus dried up and the inflammation disappeared so it enabled her to be back at the piano doing concert work the next day without material inconvenience. In all she was kept from her work only three days—the day before I saw her, the day the vaccine was given, and the day the abscess under the nail was opened.

I saw this lady later and found a new nail growing, which shows that the infection had done considerable damage. Under conventional treatment extensive infections at the root of the nail are usually very tedious. Without the use of vaccines it would probably have required from two to four weeks' time to accomplish what was done by this method in two days. To a professional musician this was a matter of very great importance.

The marked advantages from the use of vaccines in wound infections is well illustrated by the following case: This was my first experience with bacterial vaccines, Nov. 9, 1906. It was a case of palmar abscess in a man. The infection resulted from a small scratch in the palm of the hand near the wrist. Five days after receiving the scratch he applied to me for treatment. His hand was badly inflamed, very painful and swollen, and the arm was swollen

nearly to the elbow. The swelling looked very much like erysipelas. There was some pus in the small opening which I enlarged. Considering it a streptococcus infection, I gave 10 c.c. of antistreptococcus serum. The next day there was less pain, but the swelling was about the same. On the third day the pain was worse and swelling had extended. The opening was somewhat enlarged and some thick pus discharged. Another dose of antistreptococcus serum was given. On the fourth day swelling and inflammation had extended to the elbow; the abscess had burrowed deep into the palm of the hand, and extended to the tendon sheaths of the wrist. The hand was very much swollen and conditions were rapidly growing worse. Temperature now was 101 degrees F. A small amount of very thick pus was discharging from the wound. Microscopical examination of smears made from this pus showed staphylococci. A dose of stock staphylococcus pyogenes aureus vaccine was given. One day later the temperature was normal and the swelling beginning to recede. Pain was much less. From this time on the hand continued to improve rapidly. The pus became thin and less, and there was practically no pain. Four days after the first inoculation a dose of autogenous vaccine was given. Two days later the opening was somewhat enlarged, and a few pieces of necrotic tissue were removed. Seven days after the second inoculation another dose of autogenous vaccine was given. The hand continued to improve without any further surgical interference, and in three weeks from the time the first dose of staphylococcus pyogenes vaccine was given the hand was completely healed. The adhesions in the flexion tendon sheaths loosened up and the hand is entirely restored to its functional usefulness.

The results in this case were certainly remarkable. I have seen cases of palmar abscess, that were less acute and less extensive, result in a permanently crippled hand, under drainage and antiseptic treatment. When this hand

was restored to its former usefulness, as a result of vaccine inoculations, it naturally aroused my enthusiasm and I am pleased to say that subsequently similar experiences were common.

I have found that severe streptococcus infections are rather common among butchers, resulting from cuts or scratches about the hands. Many of these cases have come under my care. The diagnosis is usually readily made from the inflamed character of the wound and the red lymphatic chains extending up the arm. The use of vaccines in these cases has been uniformly successful. The following cases serve as illustrations:

A young man working in a butcher-shop slightly cut his thumb and got it infected; two days later he called a physician, who advised him to go to a hospital so that he could have his arm and hand packed in ice and receive other necessary attention. Instead of going to the hospital, he decided to change his medical attendant and came to consult me. I found the thumb badly swollen and a red lymphatic streak about three-eighths of an inch wide extending up the arm. His temperature was 99.5 degrees F. I gave him a dose of combined vaccine containing streptococcus 30,000,000 and staphylococcus aureus and albus each 100,000,000, and ordered rest in bed. The dressing consisted of hot moist gauze and bandages. The following day he felt so much better that he went to work, carrying the infected hand in a sling. Two more inoculations of the same vaccine at two-day intervals cleared up the infection, the man continuing at his work.

The following case shows what can be accomplished with the most severe types of streptococcus infection:

Mrs. H. cut her thumb slightly while paring fruit. The cut was so small that it was disregarded and not even bandaged. She dressed some chickens and infected the wound.

The next day, September 12, when I saw her, the thumb was badly swollen, cyanotic and very painful. A red lymphatic streak extended to the shoulder with the glands at the elbow badly swollen. The temperature was 100 degrees. Clinical symptoms indicated an unquestionable streptococcic infection. Since it was a skin involvement where staphylococci are usually also found, I gave a mixed vaccine containing 30,000,000 streptococci and 100,000,000 each of staphylococcus albus and aureus without waiting for a bacterial examination. By the next day, September 13, the temperature was normal, the red lymphatic streak reaching below the elbow. The thumb was still painful and swollen, the glands at the elbow were slightly more swollen but not so painful. By September 14 the inflammation on the arm was still present at the elbow glands and tissues around them, temperature normal, thumb swollen and painful. I repeated the dose of mixed vaccine. The following day, September 15, the swelling at the elbow with involved glands was rapidly diminishing and in a few days later had entirely disappeared. The thumb was still much swollen and cyanotic, the nail being blue. Around the point of infection a distinct line of demarcation appeared showing a gangrenous patch three-eighths of an inch wide and five-eights of an inch long.

The local treatment from the start consisted in keeping the thumb wrapped in a gauze bandage which was kept continually saturated with a 1-4,000 bichloride solution. This kept the feverish skin moist and at the same time acted as an antiseptic. An interesting point in this connection serves to show how little value local antiseptics really are when the infecting process has gone beneath the skin. On September 18, the dose of vaccine was again repeated. Three days after this the hand became somewhat swollen and by September 22 the temperature had again gone to 100° with much local pain. On this day 50,000,000

streptococcus and 100,000,000 each staphylococcus aureus and albus was given. On the 23rd the temperature was normal, but unmistakable signs of pus appeared in the space between the thumb and hand. A small incision was made and about one drachm of pus allowed to be discharged. After this the case progressed favorably with the exception of the gangrenous portion which required ten days to separate and come out. The slough extended down to the periosteum. The wound granulated over rapidly and healed, and the thumb was restored to its former usefulness.

The infection in this case was an exceptionally virulent one. Anyone who has had any experience with a streptococcus that will cause gangrene within the first few days of an infection knows that under the conventional treatment this patient would have at least lost her thumb, probably her arm and possibly her life.

In cases of more extensive wounds that have been cleansed, stitched up and dressed, where there is the least suspicion of an infection a day or two later, a dose of streptococcus-staphylococcus vaccine should be given. This will raise the immunizing power at once and retard or abort the infective process. I find that 30,000,000 streptococcus, combined with 100,000,000 each of staphylococcus aureus and albus, is a good average dose. Ordinarily the injection may be repeated on the second or third day. If no noticeable improvement is observed within 24 hours, double this dose should be repeated.

As a general rule, inoculations should be made at shorter intervals in cases of severe infections than in milder ones. Improvement, with a few exceptions, should be observed within 24 hours after the first inoculation.

The success attained with this method is so positive that no case of infected wound should be treated without vaccines, especially when a case is seen early in the course of the infection. This is very important. In the early stage

of an infection we are never in a position to know how the immunizing mechanism, if unaided, will respond. If the infection should be aggressive, it may spread enough to do considerable damage before the patient is seen again. Where an infection has gone on for some time and the case is progressing favorably the indications would be that natural immunity is being established, making the use of vaccine unnecessary.

It must be remembered that vaccine treatment in these cases will not in the least interfere with any local or other treatment that might be desirable. Rest in these cases of infection is always advisable. It has frequently been demonstrated that fatigue has a marked influence in lowering the immunizing powers against pathogenic bacteria.

I feel very confident that bacterial vaccines are the most valuable remedies at our command in treating infected wounds, especially when it is possible to use them early in the course of the infection.

GANGRENE.

The problem of gangrene in wounded soldiers at the French frontier during the present war has been most serious. This gangrene has been due to the bacillus perfringens and is commonly known as "gas bacillus gangrene." The organism seems to be prevalent in the soil of northern France, which accounts for so many wounded soldiers becoming infected. A polyvalent stock vaccine was prepared and used in these cases with good results.

The gangrene met with in this country is usually due to a streptococcus, and unless therapeutic immunization is instituted early in these cases a fatal termination may be expected. I saw one of these cases in an alcoholic. He was cut in the wrist as the result of a quarrel while intoxicated. The cut was considered too small to make it worth while to call a doctor. Four days later when I saw him the

arm was badly swollen, showing every indication of a serious streptococcus infection. A small dose of stock streptococcus vaccine was given at once. A specimen of the pus was also procured and sealed in a sterile vial for the purpose of making an autogenous vaccine. This was one of my early vaccine cases and on account of the theoretical objections to using vaccines in acute infections and the fear of a "negative phase" the vaccine was given very cautiously. A slight improvement was noticed the next day, after the first inoculation. Three days later an autogenous streptococcus vaccine was given. At this time the arm was very badly swollen and there was a temperature of 104 degrees F. The next day two gangrenous spots appeared midway between the elbow and shoulder. The patient was taken to a hospital, his arm amputated, but he died shortly after the operation. It is impossible to know if better results had been gained with larger doses at daily intervals. Later experiences, however, convince me that his life could have been saved if vaccine treatment had been started earlier and given in sufficient dosage at short intervals.

In one case of diabetic gangrene of two toes I had a beautiful result with a combined streptococcus-staphylococcus vaccine in that the extension of the gangrene was prevented. After the toes were amputated good union was procured.

Dr. J. V. Becelaere, of Detroit, (Bacterial Therapist, May, 1913) reports an interesting case of gangrene treated with stock vaccine. This was a man 72 years of age, but well preserved. He had been sick for a week with conditions pointing to septicemia. There was a purplish livid infiltration of the leg, on the outer ankle an ulcer an inch in diameter, and on the dorsum of the foot a gangrenous area two and a half by one and a half inches in diameter with an irregular outline, but no definite line of demarka-

tion had developed. There was much pain. Examination revealed no fluctuation so there was no indication for drainage. The responsibility for taking care of the case was reluctantly assumed because two recent previous experiences in similar cases terminated unfavorably. A mixed vaccine, streptococcus 30,000,000, staphylococcus aureus and albus each 100,000,000 was given. The next 40 hours disclosed considerable improvement in the patient's general condition. The gangrenous focus was also looking better in that it was softening, soggy, and beginning to loosen from the edges and underlying tissue. The same vaccine was repeated. The gangrenous mass became looser and at the end of the first week it was possible to remove it entirely with moderate traction. A third injection of the vaccine was given on the ninth day. After two weeks' treatment the lesion gave indications of repair going on. The vaccine treatment was continued at three to five-day intervals. During the fifth week a dose of staphylococcus vaccine 400,000,000 was given. By this time the ulcer had practically healed over. Streptococcus-staphylococcus combined vaccine was continued. Two months later the skin of new formation again broke down over a surface about an inch in diameter, gangrenous in character. The patch came away in toto, leaving a bleeding surface. The former dose of streptococcus-staphylococcus vaccine was now doubled. The healing process was rapid and in ten weeks after treatment was started a complete recovery had taken place.

BURNS.

Much can be accomplished in the care of burns by vaccine therapy both in relieving pain and promoting rapid healing. The painful condition of burns presents two distinct stages, the pain caused by the burn itself, which usually subsides during the first day and the pain caused by the infection present in the burned area from germs normally on the skin. Of course these infections depend

largely on the extent and depth of the burn. The virulence of the infecting organism and the immunizing responce of the patient must also be taken into consideration.

In these cases staphylococci are the most constant infecting organisms although streptococci are also found. Such infections are not only responsible for most of the pain, but much of the fever, rapid pulse and the depressed condition as well. Where vaccines are used in these cases a high state of immunity is established. This not only relieves the patient of much suffering but aids in the healing process as well. In deep burns, where the entire depth of the skin is destroyed, the pain caused by these infecting organisms during the time required for the destroyed tissue to separate from the living is usually quite severe. In such cases the vaccines are a decided aid. Here is an illustration: Miss S. K., working in a laundry, had her hand caught by a mangle. The hand was badly crushed and horribly burned. Before the machine could be reversed and the hand released the entire top of the hand was burned so severely that the skin, all the tendons, and a part of three meta-carpal bones sloughed away. A few days after the accident the hand became very much inflamed, swollen and painful, the inflammation showing more particularly at the margin of the burn. Considering the condition to be largely due to infecting organisms I gave a mixed streptococcus-staphylococcus vaccine. By the next day she was relieved of the pain and the swelling was not so intense. Four days later the hand became more painful again and another dose of vaccine was given with the same favorable result. Inoculations were continued at from four to six-day intervals until the slough was removed and during all this time she suffered practically no pain and was able to sleep regularly at night. With the aid of extensive skin-grafting the hand healed rapidly and a good recovery resulted.

The importance of a healthy granulating surface before

skin grafting is undertaken, so that the grafts will grow is well recognized. There is no treatment in my experience that has a more pronounced influence in promoting healthy granulation than the proper application of vaccines. If grafts are properly secured on a good granulating surface under the immunizing influence of vaccines, they will practically all grow. In my experience excellent results have been secured by employing small grafts about one-sixteenth of an inch square placed on the granulations about three-eights of an inch apart, and secured by a single layer of gauze. The one layer of gauze is securely fastened, so that it lies over the granulating surface with some tension; where practical, as in the case of an extremity the gauze should go all around and be either sewed or securely tied on the opposite side. This gauze will hold the grafts securely in place and should not be removed for five or six days; the usual dressings being placed over this gauze and redressed every day or two. I devised this method of holding grafts thirty years ago while taking care of a man who had burnt his leg by falling into a kettle of boiling potash. Nearly all the skin was destroyed from the ankle—the shoe protecting the foot—to the upper third of the thigh. By making many hundreds of small grafts and securing them as described, I succeeded in covering the leg with skin.

VACCINES AS ADJUNCTS AND PROPHYLACTORS IN MAJOR AND OPERATIVE SURGERY.

The beneficial results of surgical interference in inflammatory conditions associated with pus formation have been so generally recognized that many operators consider their duty in such cases ended when adequate drainage has been established. A self-satisfaction that everything possible has been done is often a great hindrance to progressive work. In operating on cases where pus exists there is always danger of the infection extending into the tissues opened up as a result of the operation. Many times pus cavities are

deep-seated and extensive operating is necessary to reach the seat of trouble. In all such cases the immunizing influence of vaccines is of unquestionable value. Many operators recognize the value of vaccines in septic wounds and give them after clinical symptoms indicate that the infection has extended. In a publication I notice that a surgeon had an autogenous vaccine prepared from streptococci and colon bacilli isolated from the removed appendix to be given to the patient "in case he needed it." Here is a case where the infection existed and if vaccines are of any value he needed it before clinical symptoms indicated a post-operative extension of the process to avoid such extension. A better method still is to give the patient a stock vaccine corresponding to the probable infecting organisms just after the operation. This will avoid the necessary delay incidental to making autogenous vaccines and the patient will obtain the benefit of early treatment. This method has given me such uniformly satisfactory results that I can unhesitatingly recommend it as a routine procedure.

Why is it that so many good physicians are so conservative about adopting new methods? A recent incident forcibly impresses this question upon me. A friend of my son-in-law was struck by a car and received serious injuries to the head and brain. He was taken, unconscious, to the hospital, where one of our leading surgeons had charge of him. One and a half days after the accident I was requested to call up this doctor and inquire about the patient's condition. The doctor informed me that he was still unconscious and that he had sustained a severe compound fracture of the skull with injury to the brain. I suggested a prophylactic dose of vaccine, but this was objected to on the ground that in the absence of fever there was no evidence of infection and that it would be ample time to use the vaccines if fever should develop, the doctor not realizing that an infection often advances sufficiently to do serious damage before fever develops. This doctor evidently does

not believe that an ounce of prevention is worth a pound of cure. Fever did develop in this case and the patient died. Surely this was an expensive lesson.

Vaccines are advantageously used in major wounds from severe trauma. Here the tissues have been cut, bruised and lacerated without the aseptic precautions observed on the operating table, making infections always more or less liable to occur. To give antitetanic serum when the wound was made under conditions making tetanus infection imminent is now recognized as a rational procedure. In accidental injuries staphylococcus and streptococcus and frequently infection by both organisms is always probable, and to give a prophylactic dose of combined streptococcus-staphylococcus vaccine is just as reasonable as the tetanus prophylaxis above referred to.

The following case reported to me by the courtesy of Dr. J. Walter Wood, of Port Richmond, N. Y., is a good illustration:

"On Dec. 23, 1911, I was called to attend Miss K., age 19 years, suffering from a compound comminuted fracture of the skull, having been struck by a hatchet. She was suffering from extreme shock, no pulse at wrist. She had lost a great deal of blood, and the brain was protruding from the wound. She had walked unassisted about 1,000 feet after the assault. I stuffed the wound with iodoform gauze, applied a bandage and removed her to the hospital. After arrival at the hospital, the shock was still so profound that I deferred operating until the following morning. Several splinters of bone were removed as well as a large piece about four inches in diameter, the periosteum having been stripped up. A portion of the brain tissue had to be removed in order to approximate the dura mater. I then replaced the bone, after leaving a silk-worm gut drain to the brain and another drain external to the bone. I was criticized by my confreres for replacing the bone, as they said there was nothing to nourish it. I replied that it beat all the artificial plates going.

"I then immediately had mixed vaccine, of streptococcus

and staphylococcus, injected and repeated again three times at intervals of three days. The young woman made an uninterrupted recovery, although there was a paralysis on the left side for about two weeks. She now appears to be perfectly normal. The wound healed by first intention. I credit the remarkable results in this case to the vaccine."

Through the influence of Sir A. E. Wright, millions of doses of "mixed infection vaccine" have been prepared in St. Mary's Hospital, London, and in the British laboratories, and used in the army hospitals of England and France with the result of materially reducing the dangers of the common pus infections in the innumerable wounds. In the French armies much damage was done by infections of the bacillus perfringens, producing "gas gangrene." This dangerous infection has been practically overcome by the early administration of a stock vaccine prepared from this organism.

The use of vaccines in surgical work has received much consideration in Russia. Antonovsky (Russky Vralch, 1915, Nos. 14 and 15), in a paper on the general application of vaccines, also points out that mixed stock vaccines containing the common pyogenic organisms may be given to wounded soldiers to advantage while transporting them to the hospital. He also recommends prophylactic inoculations of vaccine prior to surgical operations in both private and military practice.

Bacterial vaccines are more and more coming into use as prophylactors in operative cases where no indications of infective processes exist. It will not be long before the prophylactic vaccine inoculation will become a part of the pre-operative routine just as the blood count and the urinary test are. The absolute harmlessness of the procedure is unquestioned, and the only thing that must be overcome is the conservatism of certain members of the profession which, I am tempted to believe, often amounts to retrogression. Such conservatism, however, cannot prevent the

final recognition of the fact that vaccines may be advantageously used as prophylactors in surgical work.

In abdominal surgery prophylactic immunization should be instituted prior to every operation, by the administration of a mixed stock vaccine containing the principal infecting organisms found in abdominal infections. These comprise the streptococcus, the colon bacillus, the pneumococcus, and the staphylococcus. The procedure is absolutely harmless and can accomplish much good by raising the immunity and thereby preventing dangerous post-operative infections or extensions of existing infections. Dr. W. H. Watters (New England Medical Gazette, January, 1912, p. 16) has summed up the situation better than I could:

"One interesting subject now under investigation is the immunization of surgical patients against post-operative infection. While the great improvement noted in surgical technic during the past two decades has largely eliminated the question of sepsis, nevertheless there is always the latent possibility of such and in instances all too numerous this becomes a very active matter. In a moderate number of individuals we have immunized against staphylococcus and streptococcus and at times against bacillus coli (abdominal and vaginal operations). Following these has been absolutely no trouble from sepsis, although they were cases picked for their apparent susceptibility to such. In one a hematoma developed in the abdominal wound and from it were isolated both staphylococci and streptococci in numbers. The surgeons predicted an extensive infection, with probable secondary operation to clear out the infection. It did not cause any trouble, however, did not become purulent beyond the blood already present, and merely retarded convalescence for about a week. Further work in this kind seems well indicated."

Madden, of Cairo (Lancet, Aug. 7, 1915, p. 271), recommends the use of a pneumococcus vaccine before operating on the mouth, tongue or throat and emphasizes the advantages of giving vaccines prior to splenectomy. He also uses stock colon vaccines before operating on severe cases of appendicitis and before prostatectomy.

CHAPTER XVIII.

INFECTIONS OF THE BONES AND JOINTS.

General Consideration.

One striking characteristic of bone and joint infections is that the same micro-organisms that cause infections of the soft tissues of the body are also responsible, with few exceptions, for infections of the bony structures, and in the treatment of bone infections with vaccines it is well to keep this in mind. In the early acute stages, before surgical intervention is advisable, much can be accomplished by giving vaccines empirically on a clinical diagnosis. In making a diagnosis for the purpose of selecting a vaccine, a possible tubercle, gonorrheal or syphilitic infection should always be carefully considered, and when present, corresponding specific treatment should be instituted. When a localized inflammatory focus on some bone has persisted after an attack of typhoid fever, a possible typhoid infection should be suspected.

The most common infecting organisms of joints and bones are streptococci, staphylococci, pneumococci and colon bacilli. More rarely we have Friedlander bacilli, pyocyaneus, and diphtheroid bacilli. One characteristic symptom of acute joint and bone infection is severe pain; and as a rule, when severe acute pain comes on suddenly, it may safely be considered to be due to pyogenic organisms, and the immediate administration of a combined vaccine containing at least streptococci, staphylococci, and pneumococci is indicated. Early immunization is the most essential factor in the successful treatment of these cases. If given sufficiently early, before pus formation has taken place, the vaccine will as a rule stimulate enough anti-body production to prevent suppuration and avoid the necessity of an operation. If an operation for the evacuation of pus should become necessary, it will be found that the immuniz-

ing influence of the vaccine will promote healing with a much more rapid recovery than where no vaccine has been employed. Where operative interference becomes necessary for the purpose of establishing drainage, cultures should always be taken for the purpose of making a bacterial examination and if necessary an autogenous vaccine can then be prepared.

Errors in diagnosis are often made by the patient attributing the localized pain to an injury. Of course it is not always easy to determine just how great an injury is necessary to produce a certain amount of distress, but when the pain and tenderness is entirely out of proportion to the amount of injury sustained, especially if there should be a rise of temperature, it is fair to assume that an infection has supervened; the slight injury probably being responsible for a lowered resistance, making the infection possible. In such cases there usually exists a focus of infection in some other part of the body from which germs gain entrance to the blood and by this means cause localized infection in the injured tissues.

The surgical viewpoint that efficient drainage is sufficient and the best treatment of deep seated infections needs revision. This was most forcibly impressed on my mind while hearing a paper read last year at the Tri-State Medical Society in Chicago. The paper consisted of a case report of a young man who had an infected tonsil with an abscess. After draining the abscess a fistulous opening remained. A few months later a localized infection developed at or near the articular portion of the lower jaw. Drainage was established, bacterial examination of the pus showed the staphylococcus aureus. The infection extended to the bone of the skull; later an abscess in the brain developed. Several more operations were performed but finally the young man died. Autopsy showed that the infection had extended from the original focus in the tonsil to the brain.

This was a case where much excellent surgery was practiced, but the treatment was nonetheless poor. The infecting organism was known, but no attempt was made during months of treatment to immunize the patient against the ravages of the infecting organism by vaccine inoculations. From what is known of the immunizing influence of a staphylococcus vaccine, to allow such a case to progress month after month until death supervenes, without giving the patient the benefit of this treatment is, to say the least, inexcusable. In striking contrast to this case, although the vaccine was employed entirely too late to obtain the best results, an account of the attending surgeon's dependence on drainage as the only means of relief, is a case treated by Dr. A. W. K. Downs, of Chicago (Bacterial Therapist, May, 1915), with whom I was in communication concerning the treatment. Dr. Downs' report is as follows:

"R. B., a young man of 19 years, complained in January, 1913, of headache, and his sight began to trouble him. This trouble continued to grow worse until a year later he could not see to read. He failed in general health, lost flesh rapidly and suffered with much pain in the head. On January 26, 1914, he was operated on at Wesley Hospital, for a cyst at the base of the brain by the nasal route. Sight improved somewhat after this operation but soon got worse again. He was taken to the hospital and operated on again April 24th. He improved enough after this operation so that he could see to get about, but pain in the head continued. He soon began to grow worse again with terrible headache and frequent vomiting. By September he was totally blind. He was taken back to Wesley Hospital and again operated on September 21. Some sight came back after a few days, but then he grew rapidly worse, developing basal meningitis with apparent abscess formation. There being no hopes entertained for his recovery, he was taken home. No bacterial examination had been made of the discharge obtained from the base of the brain.

"On October 15, 1914, I was called to see him at the house and found him unconscious, completely blind in both eyes, pulse 50, and his respiration so slight that it was al-

most impossible to tell if the patient was breathing. While I was there the patient vomited and put both hands to his head. His sister said he had been doing this ever since he was brought home from the hospital.

"The only possible hope in my judgment was the use of vaccines and I told the family so. I, therefore, gave him three-tenths of a c.c. of a combined vaccine, consisting of streptococcus 100,000,000, pneumococcus 100,000,000, staphylococcus aureus and albus and citreus each 200,000,000, and colon bacillus 200,000,000 per c.c. I was afraid the streptococcus, pneumococcus and colon bacillus might have been carried in during or after the operations. The following day I visited patient and found a considerable area of inflammation at the point of injection, not much change in condition of patient. I injected the vaccine again October 20, and found patient very much improved; he was beginning to notice the difference between light and dark with the right eye, the vomiting was getting less and he was taking a little nourishment, headache a little more severe, due to focal action of vaccine, I believe.

"On October 25th, I gave one-half c.c. of vaccine, the patient was very much better; had very little vomiting and headache in the morning, and not so severe; patient able to see objects in room and difference in colors with right eye.

"November 3rd, I gave two-thirds c.c. of the same vaccine. Patient was still more improved, sight good enough in right eye to enable the patient to distinguish faces and he could see a little light with left eye; appetite much improved.

"November 8th, I gave one c.c.; at this time general condition and eyesight were much improved, but headaches worse with a return of vomiting. I concluded that my vaccine was at fault as to contents and on November 24, I changed to one-half c.c. vaccine containing staphylococcus pyogenes aureus 600,000,000, staphylococcus pyogenes albus 600,000,000 per c.c. November 27, vomiting stopped, appetite improved, eyesight was improving, he was getting some color in his face, he went out walking and felt fine.

"November 30th, complains only of a little headache. Weight and eyesight improving.

"December 3rd, staphylococcus aureus 600,000,000 only was given. Improvement very marked. Gave same vaccine every three days until December 28th, when patient was practically cured. On December 8th, I had Summerfield, optician, fit his eyes to relieve eye strain. He was now able to read large print. Eyes again fitted December 27th. Efficiency of eyes with new glasses about 80 per cent normal, could read ordinary newspaper. Good appetite, sleeps well, heart action good, gain about 50 pounds."

Dr. Downs informed me recently that this young man is now entirely well. There is no doubt in my mind that the vaccines saved his life and that if the doctor who operated on him at the Wesley Hospital had placed less reliance on drainage and more on immunization by giving vaccines, he could have effected a cure after the first operation.

I have repeatedly seen surgeons make incisions for deep-seated inflammations for the purpose of drainage where no pus was found. Streptococcus infections may be quite extensive without producing pus and when we have deep-seated infections it is often a difficult matter to determine the presence of pus even after making a blood count. Unless quite positive symptoms exist that pus accumulation is present it is better to postpone operative interference and meantime employ therapeutic immunizations with bacterins. By this means many times infective processes can be aborted and a cure established without an operation.

OSTEOMYELITIS, OSTEITIS AND PERIOSTITIS.

The organisms responsible for osteomeylitis are the staphylococcus, the streptococcus, the pneumococcus, the colon bacillus, the typhoid bacillus, the goncooccus and the tubercle bacillus. Of these the staphylococcus aureus is the most common. In the early acute stages an extensive blood infection often accompanies the bone involvement. On theoretical grounds some writers consider the use of vaccines contraindicated where such an extensive acute infection exists, and contend that if vaccines are employed, ex-

ceedingly small doses should be given, but experience shows that such theoretical conceptions are based on a false premise. Many of these cases are very toxic as shown by the temperature, pulse-rate and nervous symptoms. This shows that immunization with adequate antibody formation is retarded or inhibited by the virulence of the invading organism. To depend on the antigenic properties of such devitalizing agents is unscientific and disastrous. Antibody production to stop the ravages of the infecting organism is of utmost importance. As has been pointed out before, live virulent organisms when circulating in the blood do not arouse tissue cell activities as adequately for antibody production as when tissues themselves are involved; and when tissues are attacked by live virulent organisms the devitalizing influence of the germs hinder antibody production, and this applies most emphatically to staphylococci, and streptococci. The result is that usually extensive pus formation and tissue or bone destruction takes place before sufficient antibody production is aroused to overcome the infection. Staphylococcus infections have a distinct tendency, as shown in cases of boils and furunculosis to develop new foci of infection, demonstrating that immunization is slow of development under the influence of the live organism. This same tendency to develop new foci of infection, with retarded immunization is also observed in cases of osteomyelitis. It has been my experience, and has been abundantly verified by other observers, that the very best results are obtained when vaccines are given as early as possible in acute infections, and this holds good whether the infection involves the blood or is localized. Furthermore, to secure the best results larger doses should be given than when treating less severe or subacute or chronic infections, and the vaccine should be given at daily intervals for two or three days.

In following up the literature on this subject, I find

that where indifferent results were obtained the vaccines were employed entirely too late or when used early were given in insufficient dosage and at too long intervals. For instance, Thomas and Ivy (Applied Immunology, p. 281) chart a case of osteomyelitis with blood infection in which they contend that the use of a staphylococcus bacterin was "possibly harmful." The chart shows that the first dose was given four days after a charted record of fever, the second dose four days later and the third dose six days after the second dose. The size of the dose is not given, but from their general recommendation on dosage in acute infections I would judge that the dosage employed was entirely inadequate and certainly, in the light of later experience, the intervals between inoculations were much too long. Under the antigenic influence of killed organism injections, when tissue cells come in contact with an antigen that possesses no devitalizing properties, antibodies are rapidly produced and the more virulent type of the infection brought under control. If the vaccine is given sufficiently early the infection may be brought under control before pus formation takes place, but where pus formation has taken place drainage must be instituted by suitable surgical intervention.

Before a positive bacterial diagnosis can be made from pus examination or blood culture the patient should be immunized by giving a polyvalent stock vaccine containing staphylococci, streptococci, pneumococci and colon bacilli, in the full average dose, about twice or three times the usual initial dose, and this repeated at daily intervals for two or three days. Later, when the infection is under control, the interval is lengthened to three to five days.

If bacterial examination should show other organisms present, corresponding vaccines should be employed, and when the infection is due to staphylococcus it may be necessary to work the dose of staphylococcus vaccine up to

several thousand million organisms before a cure is effected.

PARONYCHIA.

One of the more common types of painful, and from a utilitarian standpoint, important periosteal and bone infection is the felon. Many a person has a crippled thumb or finger due to this ailment. Lancing by cutting through the periosteum gives fairly good results, but at best, it is a painful procedure and frequently the healing process is slow with a possible necrotic bone development. I have on three occasions aborted well marked cases of felon by giving streptococcus,—staphylococcus combined vaccine in the early stages of the infection. There is no good reason why this cannot be regularly accomplished if immunization is applied reasonably early.

SUBACUTE AND CHRONIC BONE INFECTIONS.

In subacute and chronic cases with fistulous openings a careful search for necrotic bone should not be neglected and when this is found, removed. Staphylococcus infections of the soft tissues near necrotic bone infections have a tendency to heal slowly even after the dead bone has been removed, but it is found that when staphylococcus bacterins are employed this tendency is avoided resulting in a rapid healing of the wound. When no dead bone is present many fistulous openings will heal under the influence of the vaccine and when healing does not take place a tubercle infection is probably at the bottom of it. Careful bacterial examinations should be made in these cases, because old fistulous openings are liable to harbor a large variety of organisms.

As a whole the results in these chronic cases are good, aside from the damage that was done by the infection before it was brought under control; at least they are much better than can be accomplished by other measures.

ACUTE PURULENT ARTHRITIS.

In the early stages of acute joint infections it is good practice to start vaccine treatment at once by giving a mixed polyvalent bacterin containing streptococci, pneumococci and staphylococci. By this means therapeutic immunization against the pyogenic organisms which cause the most damage may be secured before serious injury to the joint has taken place. If any fluid can be detected the joint should be aspirated and where pus is present drainage by opening the joint should be established. Cultural and microscopic examinations of the pus will determine the exact nature of the infection, when corresponding stock vaccines should be given; and when unusual organisms are found, an autogenous vaccine should be prepared and administered. In the early acute stages vaccines should be given at daily intervals for several days and at three or four day intervals after the extremely acute symptoms have subsided. The greatest danger as a result of purulent joint infection is destruction of the synovial membrane, resulting in a crippled or ankylosed joint. By the early use of vaccines, in conjunction with drainage, this destructive character of the infection can be avoided. Other recognized measures such as rest and suitable motion at the proper time should not be neglected.

ACUTE ARTICULAR RHEUMATIC FEVER.

Acute articular rheumatism is now definitely classed among infectious diseases. Bacterial research in this field was started by Wilson (Edinburgh Medical Journal, June, 1885), who found micrococci in the pericardial fluid of a case dying of rheumatism. Budzy (Orvosi Hetilap, 1890, Nos. 39-42) found streptococci in the joint fluid from the shoulder in a case of acute rheumatism. Extensive research has been carried on since then by numerous investigators, prominent among them being Poynton, Payne,

Wassermann, Fritz-Meyer, Triboulet, Walker, Rosenow and others.

From a careful analysis of the various findings it is clear that the disease is due to the streptococcus in one or more of its various forms, including in some instances a possible pneumococcus. The fact that many cases of rheumatism follow an attack of tonsillitis, otitis media or other streptococcus infections is taken as strong evidence in favor of the streptococcus. Gurich and Schichold (Journal A. M. A., March 19, 1910, p. 1016) have found suppuration in the tonsils almost a constant accompaniment of rheumatic affections. The germs responsible for many cases of articular rheumatism nest in the tonsil pus and pass thence into the blood.

H. Steinert, in his paper on streptococcus sepsis (Journal A. M. A., Oct. 22, 1910, p. 1510), says: "The sepsis assumes an acute form, as a rule, but in those who have had acute articular rheumatism at any time the sepsis develops in a milder, more chronic form. This suggests that articular rheumatism is a streptococcus disease and modifies the reaction to later streptococcus invasion."

From what we know of the etiology of rheumatism it is not to be wondered at that conventional treatment has had but little influence on the course of this disease. Some still give drugs, with the idea that rheumatism is caused by an excess of certain acids. Baths and bakes are usually given with the idea of sweating out the uric acid and other poisons. A deeper study of these therapeutic measures has led some to believe that heat and baths, as applied in institutional practice, cause an increased phagocytosis, and thus aid in ridding the patient of the infecting germs. Large doses of salicylates, given at short intervals, are also believed to increase phagocytosis. All these remedies work in an indirect manner and are thus of questionable value.

Many a rheumatic is advised to go to a sanatorium because the attending physician wishes to shift the responsibility.

One characteristic of articular rheumatism is the liability of the patient to relapses, and this is particularly noticeable in cases treated with salicylates. Menzer (Zeitschrift f. Hyg. u. Infectionskrankheiten, 1911, lxiii, 296) is of the opinion that the salicylate treatment is largely responsible for these relapses. He considers acute articular rheumatism a streptococcus infection, and by using the salicylates the course of the disease becomes modified in such a manner that the immunizing resistance to the infecting organism is not sufficiently developed to establish a permanent cure.

The curative value of the vaccine treatment is direct, the results obtained being entirely due to the stimulation of the immunizing faculties of the system, and, consequently, such recoveries are more permanent.

When I see the many cases of prolonged illness and absolute failures in the treatment of rheumatism with salicylates, I often wonder why physicians continue to rely on them and prescribe them so extensively. It may be argued that experience has demonstrated their value. Yes! salicylates will give relief from pain and in some cases may even shorten the course of the disease, but they certainly have no marked curative effect. The most apparent reason why physicians persist in using salicylates is because they are so accustomed to indifferent therapeutic results from drug administration that the results from salicylates in the treatment of rheumatism, though slight, are sufficiently encouraging to continue their use. I find that when a doctor has once given bacterial vaccines a fair trial in the treatment of rheumatic fever he no longer relies on salicylates.

My experience in the treatment of rheumatism by thera-

peutic immunization during the past fourteen years has been extensive. For a number of years I used antistreptococcus serum and the results of my experience were presented in papers, read before several medical societies, and published in medical journals.*

A reference to these papers will show that the results were very encouraging, especially as compared with salicylates or other conventional treatment. Because of the large protein content of antistreptococcus serum it was soon found that symptoms of anaphylaxis would develop from repeated inoculations and consequently the serum was not applicable in chronic rheumatisms where treatment was necessary over a considerable period of time. I found that in acute cases the results were, as a whole, good.

The publication of these papers naturally brought some inquiries from physicians whom I advised concerning the use of this serum in rheumatic cases. My experience with the use of antidiphtheritic serum had been extensive, and taught some valuable lessons in serum reactions. By the spring of 1907 my experience with antistreptococcus serum had also been extensive. I had found that serum reactions were erratic; no symptoms could be implicitly relied upon as a guide to determine when it was absolutely safe to repeat a serum injection to avoid a dangerous anaphylaxis.

During the fall and winter of 1906-1907 I used sufficient bacterial vaccines to appreciate their therapeutic value. From the results obtained in rheumatic fever with antistreptococcus serum I was convinced that the disease was due to streptococcus infection and, upon seeing the results from bacterial vaccines in other infections, I began to use streptococcus vaccine, prepared from streptococci isolated from cases of tonsillitis, in cases of acute articular rheumatism. I found that the results were even better than from the use of antistreptococcus serum; while at the same time,

* American Medicine, Vol. VI, No. 16, pages 633-635, October 17, 1903.
* Journal of the Michigan State Medical Society, June, 1904.
* Journal of the Michigan State Medical Society, January, 1907.

on account of the small protein content in the vaccine, the dangers of an anaphylaxis were entirely avoided. The dangers of anaphylaxis being overcome, it was found that treatment could be continued long enough to make this treatment available for chronic cases. Consequently I advised inquiring physicians to use streptococcus vaccines in the place of antistreptococcus serum and in many instances supplied them with the vaccine.

At first streptococcus vaccine was principally relied upon and somewhat later a polyvalent streptococcus-pneumococcus combined vaccine was employed, but during the past four years a polyvalent combined streptococcus, pneumococcus, staphylococcus vaccine was usually employed. This is in conformity with the practice of extensive vaccine users. As experience increases the tendency is towards employing more extensively combined preparations.

The therapeutic results from the use of streptococcus or streptococcus combined vaccine in the treatment of rheumatic fever are uniformly good both as a means of securing relief from pain as well as effecting an early cure. Here Wright's contention, that immunization relieves pain, is most beautifully illustrated. Everyone is familiar with the intense suffering that is associated with this disease. Time and again I have seen cases with intensely swollen painful joints relieved within 24 to 36 hours. A much more pronounced relief, at that, than could be secured with salicylates in the same length of time. Early application is essential to secure the best results, and cases that have not had previous attacks get well quicker than cases that have had frequent relapses under drug treatments. If the infection is very active with fever and much inflammation, larger doses should be employed and given at shorter intervals than in less severe cases. In these severe cases the initial dose should be streptococcus 60,000,000 and pneumococcus 80,000,000 and the dose repeated in one or two

days. Children should receive proportionately less. Marked improvement will almost invariably be observed after the first or second inoculation. This is especially the case if treatment is started early. After the more acute symptoms have subsided, inoculations should be repeated at three to five-day intervals and the treatment continued until all symptoms of the disease have vanished. To avoid relapses, especially in cases where previous attacks were treated with drugs, it is best to give the vaccines for a month or more at weekly intervals. When the disease presents itself in a less severe and less acute type, treatment should be started with a smaller dose, about one-half or one-third the amount given in the more severe cases, and inoculations made at two to three-day intervals. In these cases treatment should also be continued for several weeks after recovery has taken place to avoid a relapse.

Heart involvement is the great danger in rheumatic fever, resulting eventually in a fatal termination or leaving the person with a crippled heart, under drug treatment. From my observations it appears that the vaccine treatment is not only instrumental in effecting a rapid cure but at the same time avoids dangerous heart complications. This applies to children in whom endocarditis occurs frequently, as well as adults. In an experience covering many hundreds of cases only two heart affections were found. One occurred in a child, the other in an adult. Each was left with a somewhat crippled heart, but when seen last both were enjoying good health.

Dr. W. C. Wolverton (Merck's Archives, July, 1914), who has had extensive experience with the use of vaccine, in speaking of results gained from their use in rheumatic fever, says:

"As remarked before, the use of a polyvalent stock 'vaccine' prepared from killed cultures of the streptococcus pyogenes, has given, in the hands of the writer and a

number of his professional acquaintances, such uniformly satisfactory results in the treatment of acute rheumatic polyarthritis, as to give the appearance of a 'therapeutic test.' However, as we are not absolutely certain as to the specific role played by the streptococcus, I have lately been using a mixed stock bacterin containing several strains of streptococci obtained from various sources (particularly from the throats of patients suffering from rheumatism and tonsillitis), together with the staphylococcus aureus and albus, and the pneumococcus. In many cases no salicylate treatment whatever was employed, the bacterin being relied upon exclusively; yet the recoveries were startlingly prompt. In every case in which the 'vaccine' was employed there was within from three to twenty-four hours, a marked amelioration of pain, resumption of joint-function to a considerable extent, and subsidence of pyrexia; and the patients almost invariably spoke of a feeling of well-being (euphoria), and even of 'stimulation' (this, of course, in adult patients, who could describe their sensations).

"The dose of streptococcus bacterin for a child is from 5,000,000 to 30,000,000 killed cocci, according to age. The dose is given subcutaneously, with a sterile Luer all-glass syringe, and is repeated in 24 hours. A third and, if necessary, subsequent doses may or may not be necessary, as indicated by the clinical symptoms. It is well to give a medium-sized dose, at gradually lengthening intervals of from two to four weeks, after recovery from the immediate attack has taken place, with the idea of keeping the child's immunizing mechanism at as high a pitch of resistance as possible, and so guard against a recurrence of the disease, and to, if possible, establish a lasting immunity. It may be remarked here that in those cases in which I have used the 'vaccine treatment' before there was cardiac involvement, no such involvement took place subsequently; any agent which has such a prophylactic value should at once commend itself. And this treatment is free from danger."

I have seen statements by bacterial laboratory workers to the effect that stock vaccines "may occasionally" give results in the treatment of acute rheumatism but that they are not to be relied upon. Anyone capable of making such a statement certainly has not had sufficient experience with stock vaccines to be a competent judge. Such conclusions are usually based on theoretical considerations and in the absence of practical experience are not justified.

In cases where previous attacks of rheumatic fever have been treated with drugs the disease is liable to run a checkered course. After a few inoculations of vaccine prompt relief may follow and in a few some other points may start up just as acutely as if no treatment had been instituted, but if the treatment is continued the inflammation will soon pass away. Other joints may become involved in a similar way, but will soon clear up. By persistently following up the vaccine inoculations the condition will in time be brought under control. Usually three to six weeks' treatment is sufficient; some cases, however, require a longer course. Dosage and intervals between inoculations must be gauged as indicated by clinical symptoms. As a rule, larger doses at shorter intervals should be given during the acute febrile stages, and the interval extended after the more acute symptoms have subsided.

From what has been said it should not be inferred that a prolonged course of treatment is always necessary. I have frequently seen cases recover promptly and remain cured. One of my patients was a middle-aged German, proprietor of a grocery and saloon. He had had rheumatic fever every winter for eight successive years. He was usually confined to bed from four to six weeks and would then gradually recover sufficiently to take a course of baths at the Mt. Clemens mineral baths and feel fairly well during the summer, but he was never entirely free from pain in the joints. I saw the patient early in the spring of 1907. He received

seven inoculations, made a complete recovery and has had no trouble since. I frequently saw him standing behind the counter selling groceries after that, and he assured me there was not an ache or pain left. Another case referred to me by this grocer (and he referred many cases to me) was a builder of motor boats. I had known him for several years and one day met him walking laboriously with a cane. He informed me that he had been unable to attend to his business for over two years on account of rheumatism. During all of this time he had not been free from acute inflammatory attacks in one or more joints. I tried to persuade him to give the vaccine treatment a trial but he assured me that he had tried so many "cures" that he was "through trying." A few months later he came hobbling into my office still suffering with rheumatism, and asked for the treatment, stating that this grocer had persuaded him to make "one more trial." I gave him the usual dose of streptococcus vaccine and asked him to return in five days for another treatment. He neglected to call and I heard nothing more from him until several months later when he sent a patient to my office to be treated for rheumatism. On inquiry I found that he had entirely recovered immediately after the one injection. Soon after the vaccine inoculation the inflammation and pain in the joints began to leave him, he began to eat better and as he was progressing favorably he felt no more treatment was necessary. I have seen this man several times since and recently he telephoned me concerning a friend of his whom he advised to take this treatment for rheumatism. It is seven years since he received this single dose of vaccine and as he says, "not an ache or pain" remains. This case aptly illustrates how the defensive forces of the body may be so balanced with the resistance of the infecting organism that a subdued infection may continue, and that by applying a slight stimulus the defenses of the body may gain the upper hand and overcome the infection.

Much has been said about the importance of a proper diet in the treatment of rheumatic fever. When a patient is brought under the influence of bacterins the diet problem is not so important. As long as fever and other toxic symptoms prevail the digestive functions are always below par. Under the influence of bacterins febrile conditions soon subside and in these acute rheumatic fever cases it is remarkable how the digestive functions improve, simultaneously with a desire for food. With a good appetite and improved digestion, any good wholesome diet will suffice, care being taken that not too much food is allowed. The prolonged anemic, debilitated condition so often found during convalescence from rheumatic fever, following drug treatment, is not found where vaccines are employed, and relapses seldom occur after the case has been cured. If we hope to free humanity from the many cripples caused by rheumatism we must cure them before they become chronic, and bacterins certainly more nearly fulfill this want than any other agency at our command.

Dr. A. G. Huegli, of Detroit (Bacterial Therapist, Feb. 1916), relates his experiences thus:

"Acute inflammatory rheumatism has been the bane of the family physician. Pick up any textbook and the first remedies mentioned are the salicylates or coal tar products, and how absolutely inadequate these remedies are we all know. Instead of establishing an immunity they break it down, instead of creating a phagocytosis they disturb it by their intolerant action on the blood cells. Since it has been established that inflammatory rheumatism is an infective process, we must look toward an immuno-therapy for relief. The mixed vaccines are daily demonstrating their practical efficiency in this omnipresent disease and it is to be regretted that the profession undertakes the treatment of rheumatism in such a half-hearted way. Rheumatism must be treated aggressively from the onset. Patients should be placed into as favorable condition as possible. The practice of starvation and strict dieting is criminal, every effort should be made to raise their vital resistance

to the top notch, and by all means mixed vaccines should be administered, not haphazard, but regularly and, to avoid relapses, over a long period of time. A mixed vaccine containing strep., staph., pneumococcus and colon bacillus has been our main standby."

Sub-Acute Rheumatism.

Every doctor is called on to treat cases in which a more or less persistent pain is complained of in one or more joints without characteristic symptoms of acute inflammation, enlargement of joint, or other indications of an active infection. It is easy enough to tell such a patient that there is nothing materially wrong, but that does not give relief. On examining these cases I have found that there is some circumscribed area or portion of the joint that reveals tenderness on pressure, or a distinct pain on a certain motion. Such cases I always consider due to a subdued, localized infection and consequently amenable to vaccine treatment. These cases under conventional treatment often run a prolonged course and not infrequently lapse into a chronic arthritis. The results from the use of bacterins in these cases is uniformly good. A combined vaccine containing streptococcus 60,000,000, pneumococcus 80,000,000, staphylococcus aureus and albus each 200,000,000 per c.c. is preferably employed in these cases. Treatment should be commenced with 0.3 c.c. and the dose gradually increased to 1 c.c., making inoculations at five to seven-day intervals. As a rule the dose may be increased to 1.0 c.c. within three or four inoculations. In some cases all the joint soreness will disappear after a few inoculations, but more frequently treatment must be continued for several months before the trouble is cleared up.

Chronic Rheumatism.

Repeated attacks of acute rheumatic infections often create a condition in which the involved joints never en-

tirely clear up between attacks and consequently the infection becomes chronic—a condition frequently met when rheumatic fever has not been treated by the immunizing method with bacterins. In these cases we have a condition in which the immunizing faculty of the system has been severely taxed by repeated autoinoculations and consequently do not respond so promptly to the influence of a bacterin as in the early stages. As a rule they are sensitive to vaccine inoculation and consequently treatment should be started with small doses and the dose gradually increased while the reactions are carefully observed. To gain the best results it is advisable to remain short of severe reactions. By this I mean that a dose large enough to cause a rise of temperature and an inflamed area four to six inches in diameter at the point of inoculation is too large. No harm will follow such a reaction if long enough time is allowed before the dose is repeated. In such cases it is advisable to defer the next dose until the reaction at the site of inoculation has entirely disappeared. If large doses are given in such cases at short intervals the patient will be kept in a less resistant condition, resulting in no improvement. I have seen cases actually get worse under vaccine treatment in the hands of an impatient physician who is always aiming to get reactions from vaccine inoculations. Small doses carefully gauged by the tolerance of the patient and gradually increased to the full dose give the best results. As a rule, inoculations should be made at five to seven-day intervals. When improvement does not follow the first few weeks' treatment it should not be inferred that no benefit is obtained. In these cases it is often necessary to continue inoculations for several months before marked improvement takes place, and by persistently following up the treatment the cases do get better.

Chronic rheumatics, on account of prolonged infections and other unfavorable conditions, present a general debili-

tated condition with a poor appetite and inadequate digestion. An improved general health with a desire to take food and an ability to digest it is a most important asset in the treatment of these cases. A mixed vaccine containing colon bacilli in addition to the streptococci, pneumococci, and staphylococci used in the acute cases is a most valuable agent to this end. This combination is now most extensively employed in chronic rheumatism. One of the most common indications of improvement is an increased desire for food, and good digestion with a resulting increase in body weight. Fresh air, sunlight, and other measures conductive to anti-body formation should also be insisted upon.

As long as the joints are tender and swollen, manipulation or use of the joints does no good, but on the contrary irritates and aggravates the condition. After the inflammatory condition has subsided active motion to restore usefulness of the joint is necessary and it is remarkable to what extent old inflamed joints will limber up under careful manipulation and use after the tenderness and inflammation has subsided.

Rheumatoid Arthritis.

Extensive and varied investigations, to my mind quite conclusively show that rheumatoid arthritis is not due to some particular infecting organism but to a variety of organisms and indirect influences. That the disease is primarily due to infection is no longer to be doubted.

The existence of focal infections, remote from the joints, as contributors toward the joint involvements, is now well established. Some are of the opinion that toxic materials absorbed from such a focus while circulating in the blood irritate these joint tissues and in that way cause the characteristic joint involvements. This hardly looks reason-

able. If the toxic substances absorbed from focal infections were responsible for the joint irritation, all the joints of the same kind or variety would be affected uniformly and at the same time, but in these cases we often see some joints severely involved while others are practically free. The localized character of the inflamed joints, sometimes in close proximity to uninvolved joints, indicates that the infection is localized in the joint tissues. Rosenow and Billings (Journal A. M. A., Sept. 12, 1914), by means of special methods, in which scrapings of joint tissues from all classes of cases of rheumatoid arthritis were employed, succeeded in securing cultures of the infecting organisms and by this means demonstrated that the infection actually exists in the joint. That focal infections are an important factor in prolonging joint infections is clearly shown by the improvement that takes place in many cases after the focal infection is disposed of. It has been repeatedly shown that recoveries take place after removing infected tonsils, bad teeth, draining sinusus, mastoid operations, treating the teeth for pyorrhea and many other localized ailments. It is equally true that in many cases in which focal infections are eliminated the rheumatoid arthritis does not improve, and this is quite easily accounted for. A focal infection simply offers a source from which infecting organisms may gain entrance to the blood or lymph stream and by this means be conveyed to the joints where new centers of infection may develop. After eliminating the focal infection and in this way cutting off the supply of additional germs some cases may recover, but in other cases the elimination of the focal infection does not help the joint conditions because the infection already established in the joints continues to remain active.

Much stress has been placed on the importance of digestive disturbances as a cause of chronic rheumatic conditions. Dr. J. Wallace Beveridge (American Medicine, June,

1915) contends that joint inflammations are often due to partly digested or incompletely digested proteins, the result of inefficient pancreatic and other secretions which allow toxic materials to form and be absorbed and by this means cause a lowered resistance and rheumatism. It is a common experience to find digestive disturbance associated with chronic infections and in such cases the infection is the primary cause of impaired digestion.

Mutch (American Medicine, June, 1915, p. 373), from work done in the laboratories of Guy's Hospital, London, concludes that staphylococci swallowed with food are a primary factor in rheumatoid arthritis. He says:

"The determining factor in the evolution of many cases of rheumatoid arthritis is infection of the upper alimentary tract with pyogenic staphylococci. These organisms are continually ingested in food, but, unless swallowed persistently in unusually large numbers are destroyed, especially by the hydrochloric acid of the stomach, or by the intestinal secretions. I have examined duodenal chyme removed during life in a great variety of conditions, and, excluding cases of chronic arthritis, have only once been able to obtain a growth of staphylococci. In this exceptional case the patient was suffering from a staphylococcal tonsillitis at the time of operation. From these observations it is evident that ingested staphylococci do not usually reach the duodenum alive but may do so if swallowed in large numbers from some septic focus in the mouth or nose. Even such organisms as escape destruction by the gastric juice cannot give rise to chronic arthritis unless, their passage through the alimentary canal being hindered by intestinal stasis, they gain entry to the mucous membrane. The most favorable conditions for the production of chronic arthritis would thus appear to be the simultaneous occurrence of a persistent inflow of staphylococci from the nose or mouth, a low gastric acidity, and chronic intestinal stasis."

Sir Wm. Arbuthnot Lane (American Medicine, June, 1915, p. 385) ascribes rheumatoid arthritis to a toxemia

resulting from intestinal stasis which so lowers the vitality that the infection of the joints cannot be overcome. He says the disease "seems only to occur in individuals whose food supply has been polluted by being delayed for an abnormal length of time in the small intestine and by the changes which take place in it in consequence of such delay."

He ascribes this pollution to infection in the small intestine, with a resulting stagnation in the cecum. His treatment consists in making an ileocolostomy or a colectomy and finds marked improvement in most of the cases so treated. Rea Smith, of Los Angeles, (Journal A. M. A., Aug. 28, 1915) in following up Lane's work, reports fourteen cases operated on with seven recoveries and one death. He made bacterial examinations of the deeper layers of the colon after stripping off the inner membrane and found the streptococcus viridans and in some cases hemolytic streptococci. He considers the colon the port of entry for the infecting organisms that cause the joint infections in these cases.

From an examination of these various viewpoints it becomes quite clear that rheumatoid arthritis is due either directly or indirectly to a variety of infections and not to a single infecting organism. The streptococcus no doubt plays the most important role, but other pyogenic organisms must also be taken into account. All modern investigation points out that systemic invasions by micro-organisms from some focus of infection lies at the bottom of rheumatoid arthritis. Systemic invasions of pathogenic organisms are only possible when a low resistance to such organisms exists and naturally the first and foremost consideration should be to build up an immunizing resistance to such organisms and by that means make these systemic germ invasions impossible. Meantime the proper care of focal infections should not be neglected. Dental caries and

pyorrhea cavities should be taken care of, diseased tonsils should be removed, sinuses drained, necrotic bone in the ear or mastoid removed, and wherever a focus of infection exists proper local treatment should be instituted. All this attention to focal infections does not in the least detract from the importance of continuing the vaccine treatment. When a joint has once become infected that joint may be regarded as a focus from which other joint infections take place. Movements and manipulations of inflamed joints may be instrumental in scattering germs into the blood stream and thence be carried to other joints. Rosenow's work (Journal A. M. A., Nov. 13, 1915), showing that streptococci isolated from certain tissues of the body have a distinct tendency to cause infections in the same kind of tissues, when inoculated intravenously into animals, strengthens the view that this takes place clinically. Germs that have become accustomed to living on joint tissues can maintain themselves better in such tissues than in other structures and consequently when micro-organisms from localized joint involvements get into the blood they are much more liable to gain a foothold in joint tissues than in other parts of the body. So we must realize that the removal of an infected tonsil, the extraction of a diseased tooth or the removal of another focus of infection does not necessarily eliminate the danger of scattering the infection. Systemic immunization is the only means at our command to guard against such infective extensions.

Rheumatoid arthritis generally develops slowly, one joint becoming involved and successively more joints become swollen and enlarged, the onset being gradual, covering a period of months or years. From the infection, inflamed joints and a resulting inactivity, other vital functions of the body become disturbed, shown in poor digestion, constipation, lassitude and the like. In the absence of an immunity development all this has a tendency to

prolong illness. The gradual development of this disease offers abundant opportunity to institute therapeutic immunization before serious damage is done to the joints, providing treatment is started early.

When I first began to use streptococcus vaccine in rheumatism, I also used it in several cases of arthritis deformans. Not noticing any actual benefit from the first few treatments, I abandoned the cases. My brother, Dr. A. T. Sherman, of Detroit, was fortunately more persistent and began treating these patients with alternate streptococcus and staphylococcus injections, and kept it up for months. After treating them from three to six months he found that there would be an improvement.

For a time I used polyvalent streptococcus and staphylococcus vaccine with good results by continuing the treatment over a long period of time. Gradually, from my own experience and from what other extensive users of stock vaccines were accomplishing, I became convinced that a more extensively mixed vaccine containing streptococcus 100,000,000, pneumococcus 100,000,000, staphylococcus aureus, albus, and citreus each 200,000,000, and colon bacillus 200,000,000 per c.c., given in gradually increasing doses, yields the best results. Viewed from the important role played by impaired digestive functions as a part of the disease, it is easy to see why this should be so. This combination contains the principal infecting organisms concerned in focal and abdominal infections and by building up a systemic immunity against a tolerance or invasion of these organisms, the underlying cause for rheumatic arthritis has been removed.

In my varied experiences in the treatment of rheumatoid arthritis different vaccines were tried out. Many autogenous vaccine advocates have published good reports from giving autogenous vaccines prepared from organisms found

in a focus of infection. I have employed such vaccines and have also prepared many of them for other physicians. Some good results are gained by this method, but we are never sure that the organism isolated from a focal infection bears any relation to the one causing the arthritis and necessarily failures often follow this method. I have also employed vaccines prepared from the so-called streptococcus rheumaticus from cultures isolated in my own laboratory and from cultures procured from other laboratories with less marked results than those obtained from the combined vaccine previously referred to. I have also had some of my friends give these special vaccines a trial and their experience was the same as mine.

In the treatment of these chronic joint infections we must be very careful not to overdose the patient. When slow progress is made—and these cases usually progress slowly—most of us are liable to get impatient and overdo things. Cases with a long-standing chronic infection, especially so when caused by a streptococcus, do not tolerate crowding. Reactions that cause considerable infiltration at the point of inoculation and possibly a slight rise of temperature are an indication that the dose has been too large. Treatment should be started with about 20,000,000 streptococcus, 20,000,000 pneumococcus, 150,000,000 combined staphylococcus and 50,000,000 colon bacillus. If considerable reaction should follow a week should pass before the next inoculation and the dose should not be increased. Where the reaction is slight the dose may be repeated in five days. The dose should be gradually increased and the dose and intervals gauged by the amount of reactions. Usually it is not necessary to increase the dose to more than four or five times the initial dose. As a rule, inoculations at five to seven-day intervals are frequent enough, and in some cases it is even advisable to wait ten days to two

weeks. As reactions become less, the dose may be increased.

In some cases improvement will be observed after four or five inoculations, but as a rule not much improvement in the joint conditions will be observed for the first three or four months' treatment. The first marked improvement noticed in most cases is that they eat better, sleep better, digest their food well and take on flesh. After that the joints gradually improve. They are liable to have some relapses with some joints becoming worse for a time, but will soon improve again. In some cases treatment must be continued for a year or more to eventually get results. The following case offers an illustration:

Mr. A., colored, porter on a Pullman car. Had been gradually getting worse with inflamed joints for seven years. When I first saw him he had been confined to bed for three months, showing typical conditions of deforming arthritis. I gave him vaccine injections regularly for three months before he was able to sit up and be about the house. After seven months' treatment he was able to be about with a cane. Vaccine inoculations were continued for nearly two years. He returned to his work as porter on a Pullman sleeper and continued regularly on his trips for four years. He contracted pneumonia while away on a trip and died soon after he was brought home.

While using only streptococcus-staphylococcus combined vaccine, two advanced cases came under my care that were not materially benefited. It is impossible to know what the combined streptococcus, pneumococcus, staphylococcus, and colon bacillus vaccine would have done for them. Early cases have always been benefited. This disease has a tendency to progressively grow worse over a long period of years. When vaccine treatment is instituted reasonably early the progress of the disease can be stopped and the patient restored to a condition of usefulness.

GONORRHEAL RHEUMATISM.

Gonorrheal rheumatism often presents symptoms so closely allied to other forms of acute and chronic rheumatic arthritis that it is often difficult to make a diagnosis. It is not an uncommon experience to have someone contract gonorrhea who has been subject to rheumatic affections. In such cases the question naturally arises whether the rheumatism is a recurrence of the old trouble, whether it is due to gonorrheal infection, or possibly to a gonorrheal infection added to a rheumatic infection caused by other organisms. Where a history of gonorrhea exists it is always well to consider the case gonorrheal until it has been demonstrated that the joint infection is not due to the gonococcus.

Gonorrheal rheumatism is in most cases associated with a focal infection in the prostate, Fallopian tubes or other parts where mixed infections with staphylococci, streptococci, colon bacilli, pneumococci, in addition to the gonorrheal infection are common. As pointed out before, focal infections, containing pyogenic organisms, are liable to produce rheumatic joint involvement. In view of the fact that gonococci and other pyogenic organisms preferably grow side by side, in these focal infections, there is every reason to believe that gonorrheal joint involvements are often complicated by other infecting organisms besides the gonococcus. So, in treating gonorrheal rheumatism, the question of mixed infections must always be taken into account and for this reason a mixed vaccine containing gonococci, streptococci, pneumococci, staphylococci, and colon bacilli, or a gonococcus vaccine alternated with a mixed vaccine containing the other organisms, gives the best and most permanent results.

In cases of chronic arthritis the question whether it is of gonorrheal origin may often be settled by giving a large initial dose, 500,000,000 or 1,000,000,000 of gonococcus vac-

cine. If the inflamed joints get markedly worse within twelve to eighteen hours with a slight rise of temperature it is safe to conclude that the gonococcus is at least a factor in the arthritis. The fever and joint reaction will subside within a day or two, often with improvements of the joints.

When gonorrheal arthritis develops during the acute or subacute stages of a gonorrheal infection the question of mixed infections is not of such great importance so far as the joints are concerned, but the focal infection is soon complicated with staphylococcic involvement and to aid in overcoming this infection staphylococcus at least should be added to the gonococcus vaccine to be employed for acute gonorrheal arthritis.

It is now generally admitted that vaccines are the best therapeutic agents at our command in the treatment of this intractable disease, but while employing the vaccine local treatment at the focus of infection should not be neglected. Strictures should be taken care of, a pus-loaded prostate should be gently massaged and where possible the focus of infection should receive proper local or surgical treatment. To procure permanent relief it is important that vaccine treatment should be continued in conjunction with other methods until the focus from which the germs were liberated to reach the joints is eliminated.

Later experience shows that when gonococcus vaccine first came into use, entirely too small doses were employed to obtain the best results. Either when used alone or when employed in conjunction with other organisms treatment should be started with 200,000,000, and the dose gradually increased to 1,000,000,000, making inoculations at five to seven-day intervals. Where not much reaction follows injections the dose may be increased to 1,000,000,000 within four or five inoculations. Usually a dose containing 1,000,000,000 organisms is large enough for continued treatment and should be followed up for several weeks or months

after all symptoms have disappeared to make the results permanent. In some cases it is necessary to give even larger doses. I have information from physicians who state that they have given doses up to 2,500,000,000 with ultimate good results.

As a rule, improvement will be observed soon after vaccine treatment is instituted and this is particularly so where the case is not of too long standing. In some cases the results are most striking, the entire inflammation subsiding after one or two inoculations, but in such instances vaccine treatment should not be discontinued for at least a month because otherwise they are liable to relapse.

In the old chronic cases where the results are not so good there is good reason to assume that a mixed infection exists, including the same conditions that prevail in deforming arthritis, and consequently must be treated over a long period of time with a vaccine that contains the gonococcus in addition to the combined vaccine employed in rheumatoid arthritis.

MUSCULAR RHEUMATISM.

It is difficult to say whether the painful condition known as muscular rheumatism is due to an infection of the muscles or whether the soreness of the muscles is the result of toxin absorption from some other infective sources, but that the disease is due to infection is clearly evident from the results that are being obtained in the treatment of these cases with vaccines. That the same organisms that are responsible for other forms of rheumatism are also responsible for the muscular variety is also apparent from the fact that the same combined vaccines which are employed in the joint involvements are equally efficient in muscular rheumatism.

The infection being of the sub-acute or chronic variety

treatment should be started with the usual small dose. The dose should be increased as indicated by the reactions and repeated at about five day intervals. A combined streptococcus, pneumococcus, staphylococcus and colon bacillus vaccine is preferably employed. As a rule, marked improvement is observed after the third or fourth inoculation, but in some cases treatment must be continued over a longer period of time before much improvement takes place. If the vaccine treatment is persistently followed out, uniform good results are obtained.

CHAPTER XIX.

NERVE INFECTIONS.

Sciatica, Neuritis.

Conventional remedies employed in the treatment of sciatica or sciatic neuritis are as inefficient as the etiology of the disease has been obscure. Gradually, however, the infectious character of the disease is becoming apparent. From close observation we find that neuritis frequently follows such acute infections as scarlet fever or septicemia; or like rheumatism it may develop after an attack of tonsilitis, or some infective process of the mouth, nose, sinuses, middle ear or bronchi.

We now know that the streptococcus, pneumococcus and even the staphylococcus often gain entrance to the blood current from these localized ailments and through the blood these germs are carried to distant parts of the body where localized infective processes develop. This is what evidently takes place in rheumatism, endocarditis and osteomyelitis.

Germs circulating in the blood reach all parts of the body and the surprising fact is that only a comparatively small part of the body tissues become involved by localization of the infection. The muscles, constituting as they do the greater part of the body weight, are particularly resistent to germ invasion. Abscesses may develop in the muscle sheath and burrow around considerable territory, but seldom, if ever, develop in the muscular tissue itself. Lymphatic channels, synovial and serous membranes and connective tissues are particularly liable to infection.

In rheumatism the synovial membrane and connective tissues around the joints are attacked, and the infection, while often very acute, does not go on to suppuration. In the subacute and chronic types, the infection continues for a long time in the connective tissue around the joints without material change in the character of the inflammation. This class of subacute and chronic infections of connective tissues is particularly liable to take place from streptococcus infections.

No one to my knowledge has ever isolated infecting organisms from the sciatic nerve in cases of sciatic neuritis, but from this it does not necessarily follow that no infection exists. It is very difficult to isolate the infecting organisms from the connective tissues in chronic rheumatic joints and necessarily it would be much more difficult to obtain them from the sciatic nerve.

The thought has been advanced that sciatica is due to a toxemia caused by some infective process in some other part of the body. If a toxic material circulating in the blood is responsible for the nerve irritation it would appear that all the nerves should be similarly affected and not one nerve trunk only become intensely involved, while all the other nerves remain practically free from attack.

From these various considerations it would appear that the conditions found in sciatica can best be accounted for on the supposition that a subdued infection exists in the nerve, probably involving the tissue connecting the nerve bundles of the nerve trunk, caused by the same variety of organisms that are responsible for rheumatic affections of the joints.

With this conception of sciatic neuritis in mind, the application of the same combined vaccines employed in the treatment of arthritis is entirely logical and the beneficial

results obtained from their use confirms the correctness of the premise.

The results obtained appear to be in direct proportion to the length of time the neuritis has existed before vaccine treatment was instituted. When the neuritis is of comparative recent date, for instance a week or two old, improvement may be expected after the first or second inoculation, but if it is of long standing it is often necessary to continue treatment for a month or more before marked benefit is observed. This may be accounted for on the general principle that chronic infections yield less readily to immunotherapy than the acute varieties. It is entirely probable that the connective tissues surrounding the nerve bundles from prolonged irritation will in time develop inflammatory deposits and encroach on the nerve tissue with a resulting pain. If such a condition exists necessarily no marked relief from a bacterin could be expected until these inflammatory deposits are absorbed, which takes time. In the comparatively recent cases the patient should be practically free from pain within a week or ten days, but it is advisable to continue treatment for several weeks to avoid a relapse. Inoculations are preferably made about four or five days apart. In the chronic cases persistency in continuing treatment is more important than crowding dosage. In such cases inoculations should be made at five to seven-day intervals and continued over a long period of time.

In my experience I have found that a mixed stock vaccine containing streptococcus, pneumococcus, staphylococcus and colon bacillus given in the usual doses for subacute or chronic infections gives the best results.

MULTIPLE NEURITIS.

What applies to the treatment of sciatica applies equally to other forms of neuritis. I have seen cases of multiple neuritis that had undergone various forms of electrical and

other treatment without benefit, get better under vaccine inoculations. As a rule these cases of neuritis respond slowly, but if vaccine inoculations are continued for three or four months and the treatment not crowded too vigorously good results may be confidently expected. A combined streptococcus, pneumococcus, staphylococcus, colon bacillus vaccine in my experience gives the best results. Treatment should be started with the usual small dose and carefully increased while reactions are carefully observed. Inoculations should be made at five to seven-day intervals and when reactions are marked it is well to wait ten days before repeating the dose.

Zapffe, in the Journal A. M. A., Jan. 16, 1915, reports a case of sciatica in which a large variety of treatments were used for eight months without success. These treatments consisted in injecting the spinal nerve roots with alcohol, gonococcus vaccine, plaster of Paris casts, Buck's extension to the leg and extensive cauterization over the course of the nerve. These procedures gave only temporary relief. Gonococcus vaccine was given because of a previous history of gonorrhea. Examination of mouth, tonsils and other organs revealed no evidence of a localized infection. Finally a bacterial examination of the urine was made and the staphylococcus and diphtheroid bacillus were found. An autogenous vaccine was prepared from these organisms. The pain eased up rapidly after giving this vaccine and after the fourth injection ceased entirely. In all, seven inoculations of this mixed vaccine were given, resulting in a complete cure. The disease has not returned after eight months.

Dr. H. Greeley, of Brooklyn (New York State Journal of Medicine, April, 1914), treated a case of sciatica with an autogenous vaccine prepared from a throat coccus isolated from the patient's throat. The first dose was 100,000,000. No reaction followed the injection, the temperature remain-

ing normal or slightly subnormal. Double the amount of vaccine was given a week later. Some reaction followed this dose as shown by an increase of pain and a rise of 0.5 degrees F. in temperature, which subsided within 24 hours. In four days he was much better, being able to walk around in the house. A week later a third dose of 400,000,000 was given. This reacted about the same as the previous injection. Within a week's time all the pain had disappeared. A final dose of 800,000,000 was given as a precaution to avoid a relapse. After five months no sign of the malady had appeared.

Dr. A. Costales, of Brooklyn, N. Y. (Bacterial Therapist, April, 1916), reports four cases of sciatica treated with a mixed vaccine. He says: "I have used a mixed vaccine containing streptococcus 100,000,000, pneumococcus 100,000,000, staphylococcus py. aureus, albus, and citreus each 200,000,000, colon bacillus 200,000,000, in four cases of neuritis (sciatica) complicated with rheumatic pains in patients with no gonorrheal history, and it has cured them in short order.

"I commenced treatment with 5 minims, injected intramuscularly in the outer aspect of the thigh—about its middle portion—increasing the dose 5 minims until 15 minims were used. Injections were given every third day and at most only six treatments were required. The bowels were also moved with two drachms of epsom salts in hot water twice a week and meat diet was cut down to three times a week. Three were women past the age of 40 and one a man, aged 48 years. All of them were heavyweights, on the average 180 pounds."

Dr. G. A. Ehret, of Cleveland, Ohio (Medical Record, Feb. 19, 1916, p. 238), reports the following interesting case of neuritis treated with vaccines:

"Case IX.—Neuritis. Mrs. M., 46 years, American. Patient seen July 9, 1914. Neuritis in both arms. Nerves tender on pressure. Four years previously patient took

electrical treatment for same, then went to a sanatorium and remained eight weeks, returning home much improved. Remained comparatively well for a year. Returned to me in 1913 with pain much more severe than ever. I tried electricity, etc., with no benefit. Patient very constipated and usual remedies gave little relief. An X-ray of the intestinal tract showed dilatation of the stomach. In July, 1914, I suggested bacterins as last resort. July 16, 1914, I gave 10 minims of stock bacterin containing, in millions of organisms per c.c., streptococcus pyogenes, 100; pneumococcus, 100; staphylococcus aureus, albus, and citreus, each 200; colon bacillus, 200. Doses were given at intervals of five days and gradually increased to 1 c.c. Twenty-four injections were given with complete subsidence of symptoms. Abdomen massaged and strapped and constipation entirely relieved. The patient has been under observation and has remained well up to the present time."

TIC DOULOUREUX.

Four cases of neuralgia of the fifth nerve with the characteristic symptoms came under my care and were treated with vaccines. Three cases were only of short standing when treatment was started and all were completely relieved after three inoculations at three-day intervals of a combined stock streptococcus, pneumococcus, staphylococcus vaccine. One of these cases had a relapse about six months later. Three inoculations of the same combined vaccine again gave complete relief and he has been entirely free from the pain for over a year.

The fourth case was one of long standing and no marked improvement having been observed after the first few inoculations the patient became discouraged and discontinued the treatment.

Dr. A. T. Sherman of Detroit (Bacterial Therapist, July, 1916), reports the following interesting case:

"In my varied experiences with the use of bacterial vaccines I have had frequent occasions to employ them in the various forms of neuritis and neuralgia, and from the uniform good results that have been obtained there is no longer any question in my mind but that these painful nerve disturbances are due to infection. Our estimation as to what can be accomplished is often best illustrated by observing the results in an extremely bad case. It was my privilege to treat such a case, and from the fact that this patient had presumably the best treatment usually employed, it is to my mind a particularly interesting one.

"Mr. F., aged 33, had been suffering with a neuritis of all three branches of the fifth nerve, on the right side, for over two years. It appears that the motor branch of the nerve became involved early in the course of the infection because spasms of the masseter muscle was an early symptom. The condition kept steadily growing worse and, not obtaining relief, he applied for treatment at the University Hospital, Ann Arbor, Michigan, at which place he was treated for eight months before coming under my care. Spasm of masseter muscle became continuous to such an extent that liquid foods only could be taken. To facilitate feeding with a tube, two molar teeth were removed while in the University Hospital. A Gasserian operation was contemplated, but on account of a similar neuritis developing on the left side, the operation was abandoned and the patient sent home as incurable. When I first saw the case, suffering was intense. Examination of the mouth revealed no decayed teeth, pyorrhea or other mouth infections. The muscles of mastication were rigidly contracted, making an inspection of the inside of the mouth and throat impossible. He had been receiving morphine to procure rest at night, but this was discontinued when he came under my care. I started treatment in January, 1915, by giving one c.c. of a combined vaccine containing streptococcus, 60,000,000; pneumococcus, 80,000,000; staphylococcus aureus and albus, each, 200,000,000, and micrococcus catarrhalis, 200,000,00 per c.c. Inoculations were repeated at five-day intervals. Marked improvement was observed af-

ter the third inoculation, the patient being sufficiently relieved to sleep three or four hours at a time without interruption. After two months' treatment the mouth could be opened sufficiently to inspect the throat. The tonsils were not large, but looked suspicious. I took them out and found them containing small pockets filled with pus. Treatment was continued by giving the same stock vaccine in 1.5 c.c. doses at weekly intervals. Five months after the vaccine treatment was started the patient felt entirely well. It is now over a year since vaccine treatment was discontinued without any return of the neuritis."

CHAPTER XX.

MISCELLANEOUS INFECTIONS.

Typhoid Fever.

Prophylaxis.—Typhoid vaccine inoculations are now universally recognized as the best means of preventing typhoid fever. This has been conclusively demonstrated in the United States army as well as in other armies of the world. Owing to the problems of transporting, feeding and caring for large bodies of men, typhoid fever often has been the cause of more illness and deaths in past wars than the bullets of contending armies. What prophylactic vaccine inoculations have accomplished in this respect is graphically demonstrated by the small incidence of this disease among the millions of troops actively engaged in the European armies.

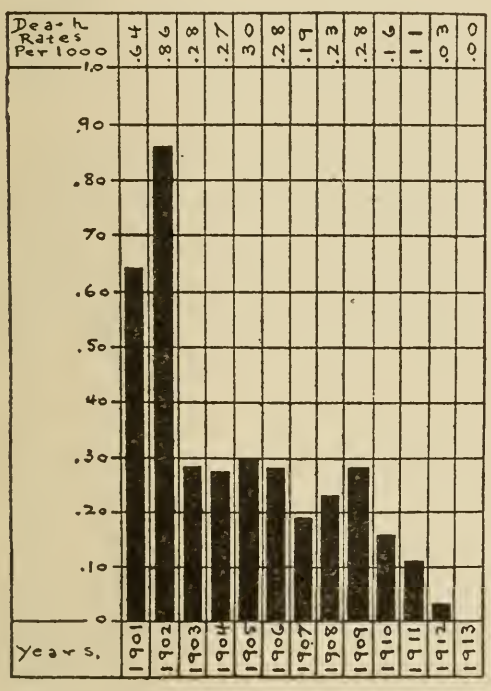


Chart 2.—Death-rates for typhoid fever, United States (enlisted men).

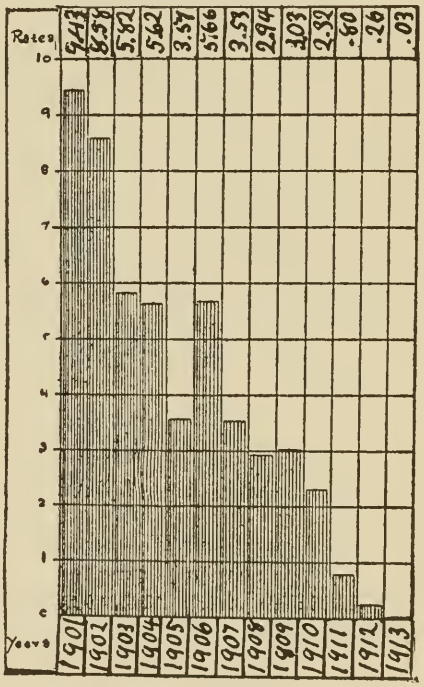


Chart 1.—Admission-rates for typhoid fever, United States (enlisted men)

The accompanying charts by Russell (Journal A. M. A., May 2, 1914, p. 1371) illustrates what typhoid prophylaxis has effected in the United States army.

What is true of army service applies equally to civil life. In any community in which typhoid fever becomes unusually prevalent, typhoid prophylaxis is instituted at once as the best means of preventing a spread of the disease. In civil life, however, immunization has not been carried to the logical conclusion of eliminating the disease, which could be done if every individual were to take typhoid vaccine, just as smallpox has been stamped out by prophylactic vaccination.

Every case of typhoid fever is a source of danger to the surrounding community because of contamination of water and food supplies, through sewers, wells, etc. Because of this, the development of individual cases should for a time, at least, be prevented, if the disease is to be stamped out.

The typhoid bacillus cannot maintain itself for more than a few months in water or unfrozen soil. The only reason the organisms remain prevalent is because of a continuous fresh supply of typhoid germs from some human being. If a general typhoid immunization were carried out during, for instance, the winter months of a given year, not enough cases would develop for the next two years to plant the soil with sufficient typhoid germs to keep the organisms in existence.

The typhoid carriers naturally would continue to be a source of danger, but by the prophylactic administration to them of vaccine they would in most instances become sufficiently immunized to cease transmitting infection. If, however, typhoid fever should develop in a community after the effect of prophylactic immunization had worn off the source of the trouble could be more readily traced to the possible typhoid carrier, and isolation or other necessary precautions promptly instituted.

Typhoid fever is largely a disease of childhood or early adolescent life, many of these cases being of the most

severe type. For this reason prophylaxis should be carried out in children as well as in adults. The dose for children is in proportion to body weight, considering 150 pounds as the average adult weight. Three inoculations should be given to confer a reliable immunity. The first dose in an adult is 500,000,000 organisms, the second—ten days later —1,000,000,000 organisms, and the third—after another ten days—1,000,000,000 organisms.

In some sections of the country paratyphoid infections are quite prevalent, and experience shows that under such conditions it is of advantage to immunize against typhoid and the paratyphoid at the same time by giving a mixed typhoid, paratyphoid A and paratyphoid B vaccine. The dosage for this mixed vaccine is, first inoculation, typhoid bacillus 500,000,000, paratyphoid A and B each 250,000,000, and for the next doses double this amount.

There has much been written and said concerning possible dangers from prophylactic typhoid inoculations. The most insistent contentions have been based on the theoretical ground that a depressed condition from the effects of the vaccine inoculation would have a tendency to make the patient liable to other infections, or possibly light up a dormant tubercle infection. The fact that in some cases a dormant focus of tubercle infection became active after typhoid prophylaxis by no means proves that the injections were responsible. Dormant foci of tubercle infections become active so frequently without any apparent cause that to ascribe an occasional case to typhoid prophylaxis is illogical.

In answering the question as to harmful results from typhoid prophylaxis, Russell (Journal A. M. A., May 2, 1914) says: "This question may be definitely and decisively answered by the plain statement that no harmful effects

have been produced." Concerning the danger from tubercle infections he says: "The table shows, also, not only that tuberculosis has not increased since the introduction of typhoid vaccination, but that it has actually decreased, as a result due, no doubt, to improved sanitation and to the care used in physical examination of recruits."

The question of reactions from the use of typhoid vaccine deserves some consideration. In my experience severe reactions have never been observed. The best reports on reactions are found in the United States Government service where exact records have been kept. Russell (Journal A. M. A., Feb. 1, 1913) devotes special attention to this question from prophylaxis in children. The following tables give the compiled results from a large number of inoculations in both children and adults. From these tables it is seen that severe reactions are not sufficiently frequent to be seriously considered.

TABLE 4.—PERCENTAGE OF GENERAL REACTIONS IN 359 CHILDREN 2 TO 16 YEARS OF AGE*

Dose	None	Mild	Moderate	Severe
First.....	73.54	24.51	1.67	0.28
Second.....	86.26	11.99	1.75	0.00
Third.....	92.56	6.38	1.06	0.00

TABLE 5.—PERCENTAGE OF GENERAL REACTIONS IN ADULTS (128,903 DOSES)

Dose	None	Mild	Moderate	Severe
First.....	68.2	28.9	2.4	0.3
Second.....	71.3	25.7	2.6	0.2
Third.....	78.0	20.3	1.5	0.1

*Comparison of Tables 4 and 5 shows that the general reaction is much more often absent or mild in children than in adults, even after the first dose, and that after the second and third doses the difference is more marked.

VACCINES IN TYPHOID FEVER.

No branch of vaccine therapy has received more favorable attention, during the past few years, than the use of typhoid vaccine in the treatment of typhoid fever, and, as investigation progresses, its pronounced therapeutic value becomes ever more firmly established.

The therapeutic application of typhoid vaccine was for some time considered irrational, on the theoretical assumption that vaccines are contraindicated in extensive acute infections, especially so when an organism is present in the blood. No doubt the wide publicity which these theoretical considerations received is responsible for the fact that notwithstanding the many favorable reports in current medical literature, many good physicians, even now, do not employ typhoid vaccine in the treatment of their typhoid cases. This aptly illustrates how theoretical conceptions, when once formed, will dominate and retard progress.

Extensive investigations by Russell (New York State Journal of Medicine, December, 1910, p. 545) and others, on the length of time required for antibodies, agglutinins and opsonins to appear in measurable quantities in the blood, show that they make their appearance in about five to eight days. Blood examinations in typhoid fever cases also show that antibodies begin to make their appearance in about eight days. From this it would appear that if vaccines are given in cases of typhoid fever, immunizing responses from the vaccine would also develop within five to seven days. Clinical experience, however, shows that enough antibody formation to favorably influence clinical symptoms, from such injections, takes place in much less time. This is particularly noticeable by the favorable influence the vaccine has on the nervous system. As a rule, the patient loses his anxious expression, feels better, looks brighter and his mind clears within one or two days after

the first inoculation. The favorable change clearly indicates that immunizing substances are developed within this short space of time. The improvement in the nervous symptoms is often seen even before any material drop in temperature takes place.

A case of mine aptly illustrates this action of typhoid vaccine. A boy 9 years old had been sick with typhoid fever for six weeks when I saw him. During the fourth and fifth weeks the temperature became normal at times, but a distinct relapse followed and when I first saw him the temperature ranged from 102.5 in the mornings to 104 in the evenings. He was delirious and did not recognize his parents, had an anxious expression, was very much emaciated, with a pulse that was rapid and poor in quality. Conditions looked very unfavorable. I gave him a 200,000,000 dose of vaccine and had the ice-bag on the head continued. No other treatment was employed. For three days after the first inoculation there was no material change in temperature but his mind cleared, the delirium subsided and the anxious expression left him. At that time a second dose of 250,000,000 was given. One day after this dose the temperature was 100 and a day later, five days after the first inoculation, the temperature became normal. On the sixth day a 500,000,000 dose was given. The case continued to improve and made an uneventful recovery.

No negative phase or bad effect from the therapeutic use of typhoid vaccines has been recorded by anyone, but on the contrary some apparently hopeless cases are reported in which large doses of vaccine were given with a resulting recovery. The consensus of opinion is that to obtain the best results the vaccine should be used early. Typhoid fever being a disease in which a diagnosis is not readily made from clinical symptoms in the early stages, the question of laboratory tests naturally arises. The

Widal test is quite reliable, but unfortunately it is not available in the early stages, before agglutinins have been formed. A bacterial examination of the blood appears to be the most reliable method of making an early diagnosis. This method is comparatively simple, but it requires laboratory facilities which are not always at hand for making immediate examinations, especially in small towns or the country. Early treatment being essential to obtain the best results, the vaccine may be advantageously given before verifying the diagnosis by blood examination. The vaccine is entirely harmless and would be followed by no bad results even if some other febrile disease should exist. Widal tests are not reliable after giving typhoid vaccine because it results in the production of agglutinins which would respond to that test. Stock vaccines prepared from an old culture, selected for its antigenic properties, give the best results. Autogenous vaccines have been extensively employed, but no one has demonstrated that they serve any better purpose than stock preparations.

There is still some difference of opinion on the question of dosage, good results being obtained from small as well as large doses. In Chapter V, on "Dosage," I pointed out that therapeutic results may be obtained from a large variety of doses inside of fairly well defined limits. The initial dose varies anywhere from 50,000,000, as advocated by Watters, Petrowich, Sample and others, to 500,000,000, as often employed by Krumbhaar and Richardson. As a whole, the tendency is towards using larger doses. I have secured the best results by starting treatment with 250,000,000 and increasing the dose by 100,000,000 or 200,000,000 at each successive inoculation until a dose of 1,000,000,000 organisms is given. At first, while there is considerable fever, injections should be made three days apart, and after the temperature goes down to 100 degrees F. or less, inoculations should be given at four or five-day intervals, with

increasing doses. After the temperature becomes normal it is important that the vaccine treatment be continued by giving 500,000,000 to a dose at weekly intervals for two or three weeks to avoid a relapse.

When vaccine treatment is started early, a permanent normal temperature with other indications of convalescence is often procured by the twelfth or fifteenth day of the disease. In cases with extreme symptoms from the start, the tendency is to modify the disease so it will run a milder course. In such cases, treatment should be vigorous from the start. A high temperature, delirium or other toxic symptoms are no indication that vaccines should be given timidly. Reactions from a vaccine injection are less marked in these cases than in the milder forms. The usual initial dose is given as soon as possible and a larger dose repeated two days later. After this the treatment is carried out in about the same manner as in the less severe cases, but as a whole the doses should be somewhat larger.

If no material improvement is obtained from two or three inoculations, the question of a mixed or paratyphoid infection should be carefully considered. If there is a reasonable suspicion that a paratyphoid infection is present it is better to give a combined typhoid, paratyphoid A and paratyphoid B vaccine than to postpone treatment until a definite diagnosis can be obtained by bacteriological tests. The dose of this mixed typhoid and paratyphoid A and B is the same for the typhoid bacillus as when this organism is used alone and the combined paratyphoid A and B should be equal in number to the typhoid organism. Thus, if 300,000,000 typhoid bacilli are given, the number of paratyphoid A and B should each be 150,000,000. The mixed typhoid vaccines are usually marketed in suspensions of this proportion, so when giving the combined vaccine the dose may be gauged by the number of typhoid organisms in the suspension.

When vaccine treatment is delayed until the second week of typhoid fever the results are less pronounced in that the course of the disease is not materially shortened; but the symptoms are modified and as a whole the patient is materially benefited. Even in extremely advanced cases, vaccines are not contraindicated, nor is it necessary to give especially small doses here. Frequently, the additional antibody production from a vaccine injection in such a case is sufficient to turn the tide in favor of the patient.

Complications.

Fatalities from typhoid fever are most frequently due to complications, especially perforation, hemorrhage or pneumonia. These complications may be due directly to the typhoid bacillus, but no doubt in a large majority of cases the usual pyogenic organisms are principally responsible as secondary invaders. The colon bacillus, staphylococcus and streptococcus normally present in the bowel live and grow side by side with the typhoid bacillus. After the typhoid infection has localized in Peyer's patches with a resulting inflamed area, these tissues become susceptible to attack by these pyogenic organisms, which in turn become an important factor in the ulcerative process, leading to perforation or intestinal hemorrhage. In a complicating pneumonia, the pneumococcus and streptococcus are also important factors. To treat typhoid fever with typhoid vaccine and disregard these secondary invaders does not give the patient all the advantages that may be obtained from immunotherapy. In all cases of typhoid fever, where bowel infections are a prominent symptom, and in cases where chest examinations show a bronchial or other pulmonary infection, a combined vaccine containing colon bacillus 80,000,000, streptococcus 40,000,000, pneumococcus 40,000,000 and staphylococcus 150,000,000 should be employed as an initial dose in conjunction with

the typhoid vaccine, and the dose gradually increased to three or four times this amount, inoculations being made at four or five-day intervals. To avoid conflicting reactions it is preferable to give this combined vaccine about two days after having given the typhoid vaccine. In case of an active pneumonia, with high temperature as the result of lung involvement, the combined vaccine should be given at one or two-day intervals until the pneumonia is brought under control and then at longer intervals. I have employed this combined vaccine in complications of typhoid fever with unquestionable beneficial results. The vaccine is well tolerated and does not in the least interfere with the beneficial effects of the typhoid vaccine, but on the contrary is a valuable adjunct treatment.

EXTRACTS FROM CURRENT LITERATURE.

The therapeutic value of typhoid vaccine was aptly brought out in an editorial in the Journal A. M. A., June 26, 1915, p. 2140, from which I will quote as follows:

"The clinical data in the literature pertaining to this phase of the treatment of typhoid fever have recently been reviewed by Krumbhaar and Richardson, of Philadelphia. This analysis includes more than 1,800 cases, and in 95 per cent of these favorable results were observed. Thirty-five of the thirty-nine observers concluded that the vaccine was useful as a therapeutic measure. In almost all instances the course of the infection was favorably influenced, and in many series the mortality was reduced. In a series treated by Petrowitch, the mortality was 3.2 per cent, as compared with 8 per cent in 220 unvaccinated patients. Krumbhaar and Richardson[1] used vaccines in the treatment of 93 typhoid patients in the Pennsylvania Hospital during the past three years. Their results were so promising that they consider the use of vaccines an important procedure in the routine treatment of the disease. The symptoms were rarely altered beyond a transitory rise in temperature;

[1] Krumbhaar, E. B., and Richardson, R., Am. Jour. Med. Sc., 1915, cxlix, 406.

but relapses and complications were diminished in frequency, and when vaccine treatment was instituted early in the course, there seemed to be a favorable influence exerted on the intensity of the infection. Since agglutination is often absent during the first two weeks of the attack, these investigators assume that antibody formation is often delayed, and that by the use of vaccines an early activity of this process can be brought about. The experiments of Gay and Claypole also suggest that there may be a hyperleucocytosis following the injection of a vaccine during the course of typhoid fever. Should these experiments receive confirmation, a good theoretical basis would be afforded for vaccine therapy in typhoid.

"The type and dosage of the vaccine have had no apparent influence on the results obtained. Sensitized vaccines have been strongly advocated by Besredka, Metschnikoff, Barbat and others, and on theoretical grounds such vaccines would be favored; but the majority of investigators have had good results with suspensions of dead bacteria prepared according to Wright's method. Although autogenous vaccines generally have been preferred, stock vaccines prepared from organisms selected for their high agglutinogenic power have been efficacious in the hands of many. Reports, however, have been so uniformly favorable with all preparations, that it seems as if the type used is of secondary importance. The dosage has also varied widely with different investigators. Semple, Waters, Petrowitch and others used small doses, while Foster, McArthur, Fletcher and Meakins obtained equally good results with large doses. Krumbhaar and Richardson gave 500,000,000 as an initial dose and two or three larger doses at short intervals. They conclude that their results were more favorable in the cases in which large doses were given. The dosage, however, must be gauged by the general condition of the patient. When the patient is very toxic, only small amounts of vaccine can be used with any degree of safety. Previous mention has been made of the remarkable results obtained by Ichikawa from the intravenous injection of sensitized vaccines.[2] Using this method of

[2] "Present Status of the Vaccine Treatment of Typhoid Fever," Current Comment, The Journal A. M. A., Feb. 6, 1915, p. 518.

inoculation, he was able to produce a rapid drop in the temperature to normal and often an early recovery. In his cases, mild intestinal hemorrhages occurred in a few instances following the injections; but these hemorrhages were no more numerous than in the unvaccinated patients. Subsequent investigators[3] also report favorable results from the intravenous method of administration of the vaccine, but they strongly emphasize the danger of a severe general reaction in some instances. Signs of collapse, severe diarrhoea and intestinal hemorrhages are complications which have occurred simultaneously with the rapid fall in temperature, and in a few instances there was an unfavorable termination. The ultimate value of this method of administration of vaccines, therefore, is a question which further observations must determine.

"Including the recent encouraging reports of Goldschneider and Aust,[4] Rhein[5] and others, the clinical evidence now at hand is derived from careful observations on about 3,000 cases of typhoid fever treated with vaccines. In almost all instances it seems that some degree of favorable influence could be noticed from their use. The observations of Elmer[6] indicate that vaccines will not prevent the attack, once infection has begun; but it seems probable that their use early in the course of the disease modifies the duration and intensity of the attack. Furthermore, in complications, especially localized typhoid infections such as periostitis and cholecystitis, and in the treatment of typhoid carriers, vaccines are of limited value. In local infections in which there is a secondary invading organism, as in pneumonia and otitis media, typhoid vaccines are probably contra-indicated. * * *"

In the editorial columns of The Lancet (Dec. 11, 1915)

[3] Biedl: Wien. klin. Wchnschr. 1915, xxviii, 125. Paltauf: Wien. klin. Wchnschr., 1915, xxviii, 125. Sladek and St. Kotlowski: Wien. klin. Wchnschr., 1915, xxviii, 389. Reibmayr: München. med. Wchnschr., 1915, lxii, 610.

[4] Goldscheider and Aust. Deutsch. med. Wchnschr., 1915, xli, 361.

[5] Rhein, M.: München. med. Wchnschr., 1915, lxii, 427.

[6] Elmer, W. P.: "Study of a Recent Typhoid Epidemic, with Especial Reference to the Use of Antityphoid Vaccines," The Journal A. M. A., April 3, 1915, p. 1147.

there is a discussion of some interesting results which have been recorded by Antonio Paginoli in Il Morgagni (Oct. 31, 1915). The reports and temperature charts which accompany this communication certainly invite further attention to therapeutic measures which seem to be effectual and free from harmful consequences. Paginoli recommends the intravenous method of administering the vaccine, for while he admits that rigor and a rise of temperature followed the injection in all cases, within 24 hours there was a crisis with profuse perspiration, and a single injection was almost always sufficient to obtain a favorable result, rapid and even surprising. The dose employed was less than has been used by hypodermic injection and Faginoli gave from 150,000,000 to 300,000,000 organisms, but prefers the larger of these as the small dose frequently necessitated a second injection. Another interesting fact brought out in this communication was that in typhoid fever, on the twentieth day, a single intravenous injection of 100,000,000 B. coli produced a crisis with a permanent fall of temperature and quick recovery.

Dr. W. P. MacArthur (The British Medical Journal, July 25, 1914) gives his experience in 63 cases of typhoid fever treated with vaccine. The causative organism was isolated in 61 out of 63 cases. In the two remaining cases the organism was not found but there was little doubt as to the diagnosis. Forty-five of the cases belonged to the "favorable" and eleven to the "unfavorable." Two cases died, making a mortality rate of 3.1.

As to results, he says:

"The results in the cases under treatment early, were most striking. There is no doubt that the disease was rendered definitely milder, and most of the patients progressively improved from their first or second injection. Three showed a constant and progressive fall of temperature after each injection, but this marked sequence was not a usual feature. The most striking point was the ab-

sence of symptoms other than the pyrexia; the headache, lumbar pains, abdominal distress, etc., disappeared, and the patients felt well and slept well; they did not look ill. In the words of one Mauritius practitioner, 'My vaccinated enterics give me no anxiety.'

"From such small numbers it cannot be said that the disease was distinctly cut short, although there seemed to be clinical evidence of this in several instances; certainly the period of convalescence was markedly shortened owing to the mildness of the course and the freedom from distressing symptoms and complications.

"These remarks apply especially to the 'favorable' group; the advantages of vaccine treatment in the late cases were much less marked, and sometimes there was no appreciable benefit whatever. In spite of the small actual numbers, the distribution of deaths, complications and relapses in the 11 late cases and the 52 others respectively, is significant. In no case did the treatment cause any appreciable ill effects."

Drs. Wiltshire, Cantab, and MacGillycuddy, of London (The Lancet, Sept. 25, 1915), relate some interesting experiences with the use of typhoid vaccine in the treatment of typhoid fever from which they draw the following conclusions:

"1. Stock typhoid vaccine is a valuable therapeutic agent for the treatment of typhoid fever.

"2. The treatment should be started as early as possible with an initial dose of 250,000,000.

"3. A reasonable suspicion that a patient is suffering from typhoid fever is sufficient indication for commencing vaccine treatment.

"4. The treatment is quite harmless to patients who may subsequently be proved not to be suffering from typhoid fever.

"5. An interval of three days should be given between doses. Shorter intervals are not well tolerated. When a longer interval is given, if four days the dose should not

be increased, if over four days the dose should be reduced.

"6. Great care must be used in dosage if secondary infections of the lung are present. If possible, the typhoid vaccine should be combined with a vaccine suitable for the secondary infection.

"7. Doses should be continued for ten days after the temperature is normal as a preventive against relapse.

"8. Preventive inoculation exerts slight, if any, influence on subsequent vaccine treatment."

Intravenous Vaccines in Typhoid Fever.—Joseph L. Miller, of Chicago (Illinois Medical Journal, January, 1916), reviews the literature on the use of bacterial vaccines in typhoid fever since it was first used by Fraenkel as far back as 1893. He finds it is impossible to place much reliance upon statistics as they vary so much, and one cannot draw definite conclusions as to the resulting reduction in the mortality. It appears, however, that the intensity and duration of the disease are markedly lessened.

The one striking feature of this treatment is the immediate and permanent interruption of the fever. Miller recommends an initial dosage of 300,000,000 bacilli. A crisis may follow a second or third injection of the same or a larger dose. One expects quite a violent reaction with a chill following the injection, and though this is somewhat alarming, it is apparently not dangerous.

Dr. Edward Waitzfelder (New York Medical Journal, Feb. 26, 1916) relates his experiences with the use of typhoid vaccine at Gouverneur Hospital, New York City, with some case reports. One case in a pregnant woman is of particular interest because the benefits derived from the vaccine are so apparent:

"Case 1.—Helen E., aged 21 years; six months pregnant. I felt this was one of the most important in the series on account of the likelihood of abortion and the high mortality which accompanies that complication. I gave the case much thought and finally decided that the increasing

toxemia and increasing temperature were more apt to induce abortion than the bacterins; so on the fourth day I gave 300,000,000 bacterins intramuscularly; at this time the temperature was 103 degrees F. This was repeated every day for eleven days, the dose being gradually increased to 450,000,000 bacterins. The toxic symptoms disappeared, the temperature gradually fell and became permanently normal on the sixteenth day after beginning treatment. At the time of her discharge from the hospital the fetal heart was quite distinct and intrauterine fetal movements were active. (Two days ago I heard that pregnancy had been uninterrupted and she was waiting for labor to begin.)"

Concerning the general advantages from the use of typhoid vaccines, he says:

"From this limited experience I am inclined to think the administration of bacterins in typhoid fever is of service, in that it lessens the toxic symptoms, viz., fever, cardiac weakness, delirium, and exhaustion. I include the latter symptoms because, in the control cases and in those previously treated with high calorie diet, without bacterins, exhaustion was more marked and prolonged. A number of the cases showed signs of cardiac depression at the time of admission or shortly after; this was materially improved within a few days after the use of the bacterins and in no case was it a factor in the third or fourth week, ordinarily the time when it is most marked and dangerous. The delirium also rapidly lessened in duration and severity. Three patients who were in high delirium on admission, with irregular heart action and cyanosis, became rational about a week after treatment was commenced. As to the temperature, I am somewhat in doubt. I cannot agree with Callison that the duration was shortened, but I am inclined to think the severity was lessened and in no case was it higher after than before the use of bacterins.

"In presenting this report, made from the hospital charts and my observation of the cases, I must confess that I am strongly biased in favor of the treatment. It is logical, scientific and exact. It measures up to and beyond the expectant plan of treatment, the one in present use, in that it reduces mortality and shortens the period of illness, and I

feel that when a more extensive experience has determined the proper dose, the use of bacterins will become the rational and adopted treatment of typhoid fever."

Dr. James G. Callison (Medical Record, June 24, 1911, p. 1127), after reviewing the literature on typhoid vaccination and reporting a series of 24 cases, says:

"A point deserving considerable emphasis is the other treatment to accompany vaccine therapy. If there is any rationale for vaccine treatment it is in the fact that it is an effort to follow or imitate Nature's method of bringing about a cure. All other treatment is admittedly symptomatic. Routine it may be called, but it is routine only in the sense that long experience has proved that certain routine most nearly meets the symptoms as they arise or prevents their development. If a vaccine will abbreviate the natural course of the febrile period, leaving it otherwise the same, then by all means the routine treatment should be continued until the vaccine controls the disease process. This has been the procedure in all these cases. The vaccine and routine treatment have been in different hands, and each has proceeded independently of the other.

"The Value of the Treatment.—The almost universal testimony as to the value of vaccine treatment given by the long list of those who have used it, a testimony the more positive the longer the list of cases treated, must certainly carry weight. To attempt to form an unbiased judgment of its efficacy is, however, more difficult. This much may be said with assurance: I believe that it is as effective or more so than the cold baths and packs. Two things seem fairly certain: It does lessen complications and reduce the number of relapses. Grant these, and the argument for its use ceases. Any treatment that accomplishes these two things must shorten the average duration of cases and reduce the death rate. * * *

"May the Vaccine Do Harm?—A question of vital importance is: May the vaccine treatment injure the patient? Almost every article on vaccine treatment emphasizes the danger of a vaccine treatment in excessive dosage, without making it clear as to what constitutes too large a dose. Too vigorous a treatment in any line certainly would be

unwise, but my experience has led me to believe that the danger line is far removed from the rational dosage. Two of my cases in particular bear on this point: Mrs. A. P., Case 17, was exceedingly toxic from metabolic products which the kidneys failed to eliminate, as well as from typhoid toxins, and examination of the urine showed a most alarming condition of the kidneys; yet her improvement was most remarkable under vaccines pushed more vigorously than in any case up to that time. Mrs. M. M. C., Case 23, was making steady progress downward and her case was said to be hopeless. The vaccine treatment was pushed, yet without injury. Her condition was such that the least added burden would have proved fatal, and yet she progressed slowly to a cure."

On the treatment of typhoid fever with vaccine, Dr. James M. Phalen (Journal A. M. A., Jan. 6, 1912, p. 11) says in part:

"Inoculation shortens the fever period and the total duration of the disease; it reduces complications and relapses markedly; the mortality of all cases that I have been able to find reported is 4.9 per cent. A distinct crisis following the second inoculation is reported by Meakins and Foster, of Montreal, to take place in 50 per cent of their cases. It is interesting that these men gave the largest dosage of the vaccine—from 1,000,000,000 to 2,000,000,000 bacilli. Very pronounced amelioration of headache, gastrointestinal symptoms and toxemia is usual. It has apparently been directly life-saving in a few all but hopeless cases, though ordinarily it has little effect on such. All agree, however, that even in the cases in which it causes no improvement it has done no harm. The negative phase of Wright, which did so much to retard progress in typhoid immunization, is non-existent except in the most excessive dosage of the vaccine. In few cases reported was there any increase of temperature following the treatment, and in none was there any aggravation of the disease. The dosage employed in the earlier cases usually ran from 10,000,000 to 100,000,000. With increasing confidence the dosage has been increasing, until at the present time it is usually from 100,000,000 to 500,000,000. It is probable that those who have reported negative or discouraging results

have been using the vaccine in too small dosage and that, with increasing dosage, even better results than thus far reported will be obtained."

One of the "Collective Abstracts" (Interstate Medical Journal, October, 1915) concerns the consensus of opinion in recent medical literature as to the value of typhoid vaccines, in which the following deductions are made:

"1. The production of antibodies or protective substances, in response to the inoculation of a bacterial vaccine, follows definite fixed laws, regardless of whether the vaccine is given for prophylactic or curative purposes; and the results in treatment must be interpreted in the light of what is known of these laws.

"2. Inoculations of vaccine in typhoid fever prevent relapses and lessen complications, and in some cases probably also shorten the original attack. Every case of typhoid fever should receive vaccine treatment as soon as the diagnosis is made, and this treatment should be continued until the temperature becomes normal, or it is demonstrated that the case will not respond to this form of treatment.

"3. Stock vaccines should be given in preference to autogenous vaccines in typhoid. The older the culture the better. When given in therapeutic doses, such stock vaccines are without injurious effect, and do not interfere with other treatment.

"4. The routine treatment should be continued until the fever process is controlled by the vaccines.

"5. The dosage used by many of those who have treated typhoid with vaccines in the past has been too small to secure the best possible results."

In individually regulated doses, the repeated injection of typhoid vaccine, according to Reiter (Deut. Med. Wochenschr., Sept. 16, 1915), does not aggravate the conditions. This is contrary to the opinions of some, but this writer finds that in most cases this procedure abbreviates the course of the disease and reduces the mortality.

In cases reacting favorably to this method, there is an early reduction of temperature; and where this does not occur it may be considered as an unfavorable prognostic sign. Reiter is convinced that the results which follow the application of typhoid vaccination in therapeutics are sufficiently good to add this treatment to the other generally accepted methods of treating typhoid fever. Repeated small doses of the polyvalent vaccine are preferable to a single large injection.

SCARLET FEVER.

The bacteriology of scarlet fever has been very carefully studied with the view of finding a specific etiologic infecting organism of the disease.

Dr. A. E. Vipond, of Montreal (Merck's Archives, Sept., 1911, p. 278) announced the discovery of a bacillus which he isolated from the lymphatic glands of cases of scarlet fever and which he considered the specific organism responsible for the disease. He reports considerable work done with the organism in the way of culture growths and animal experiments; five monkeys and two rabbits developing symptoms of scarlet fever including the rash. The same organism was again isolated from the lymphatic nodes of each animal and grown on culture media with the same characteristic growth. No further investigations along this line have come to my notice.

Drs. Guy L. Kiefer and U. S. Ferry, of Detroit (Medical Record, May 23, 1914), report some prophylactic and clinical results from a vaccine prepared from an organism which they designate the micrococcus "S," isolated from the nasal mucous membrane in scarlet fever cases. Their results would indicate that the organism possesses some specific properties in relation to scarlet fever, but I have not observed reports of further work along this line.

Streptococci a Pathogenic Factor.

The fact that streptococci are found in the blood of so many cases of scarlet fever, and the presence of strptococci in the urine, especially when complicated with nephritis, and in cases of severe adenitis, is conclusive evidence that this organism is a most important etiologic factor of

In a paper on the bacteriology of scarlet fever (Journal A. M. A., May 29, 1910, p. 1803, review Wiener Klinische Wochenschrift, April 15, 1910), "Schleissner found streptococci almost in pure cultures on the tonsils in every case of scarlet fever examined in its incipiency before the sore throat had developed. He was also able to cultivate streptococci from the blood in a large proportion of the 73 cases reported, and the presence of antibodies was also unmistakable, reaching the maximum about the tenth day. It seems evident that streptococci are closely connected with the scarlet fever process, and hence that antisterptoccoccic treatment can not fail to aid in attenuating the disease."

My own personal experience is limited to eighteen cases. Three of these were very bad cases with extensive throat complications in the early development. The promptness with which they recovered after injection of streptococcus vaccine indicated unmistakable evidence of the value of the vaccine treatment. One case was complicated with nasal diphtheria. In this case I used streptococcus vaccine in conjunction with liberal doses of antidiptheritic serum but after apparent improvement for several days the patient finally died on the tenth day. All the other cases recovered without any of the unpleasant results that so often follow this disease.

Others using streptococcus vaccine in scarlet fever have obtained similar encouraging results. From what information I have been able to collect it seems to me that every case of scarlet fever should have a dose of streptococcus

vaccine as soon as a diagnosis can be made. Such a procedure unquestionably modifies the course of the disease and there is freedom from streptococcus complications.

In my early cases treatment was started in adults with a dose of 30,000,000 and in children with proportionally less, but from later experience in the use of vaccines in extreme acute streptococcus infections I am satisfied that double this dose may be employed to advantage.

In all the reports I have noticed in which indifferent results were recorded from the use of vaccines in scarlet fever, either insufficient doses were employed or the intervals between inoculations were too long. Thus, Dr. Donald Macintyre (abstract in New York Medical Journal, March 20, 1915) reports 100 cases of scarlet fever treated with a combined vaccine of streptococcus 50,000,000 and staphylococcus 1,000,000,000 to a dose at seven-day intervals. On comparing the length of time the vaccinated cases remained in the hospital with the hundred control cases it was found that the vaccinated cases on the average got out half a week sooner. Such a showing is not liable to arouse any enthusiasm. If the vaccine had been given at one-to three-day intervals, I am confident better results would have been secured.

The staphylococcus is often a complicating infecting organism where streptococcus infections are present. For this reason it is of advantage to employ a combined streptococcus-staphylococcus vaccine in the treatment of scarlet fever.

In adults the initial dose should be about 50,000,000 streptococcus and 200,000,000 staphylococcus, and children should receive from one-fourth to one-half this amount. The more severe cases must be treated vigorously by giving larger doses and at shorter intervals. In those with high temperature and other toxic symptoms, a full dose

is given at once and repeated at daily intervals for two or three days. After the temperature has subsided the inoculations should be made at three- or four-day intervals. In the less severe cases, somewhat smaller doses may be employed and inoculations repeated, two to four days apart.

As in all other severe acute infections, early treatment is most important for the best results. Often the diagnosis is not clear. Where in the early stages—before a rash has appeared—there is reason to suspect diphtheria, a dose of diphtheria antitoxin must be given in conjunction with the vaccine. By this means the dangers of diphtheria as well as those of scarlet fever may be obviated.

PROPHYLAXIS.

Just as the use of typhoid vaccine as a prophylactor has given such satisfactory results, so the use of streptococcus vaccine is useful in the prophylaxis of scarlatina. Since no harm can result from a prophylactic injection of vaccine every child and adult exposed to scarlet fever ought to be inoculated preferably at the earliest possible moment. There is no reaction, no inconvenience and no trouble whatever, after giving these injections.

I have used a streptococcus vaccine as a prophylactor in eight children exposed during the entire course of the disease of another member of the family. Of these two contracted the disease in a very mild form.

For prophylactic purposes rather larger doses of streptococcus vaccine are employed. The first dose should be 100,000,000 and the two subsequent doses 200,000,000 at seven-day intervals.

Watters (Journal A. M. A., Feb. 24, 1912, p. 546) employed a vaccine prepared from throat cultures in cases of scarlet fever for the prophylactic inoculation of 21 nurses who had not had scarlet fever prior to going on duty in a scarlet fever hospital. Of these one contracted the disease.

Of fourteen other nurses who were not inoculated, five came down with scarlet fever.

Dr. Ernest E. Irons (Journal A. M. A., Nov. 12, 1910, p. 1718), in speaking of vaccines as prophylactors, says: "The prophylactic use of streptococcus vaccine in scarlet fever is receiving much attention, particularly by Russian physicians, whose satistics appear to show a remarkable immunity to the disease in those who have received the protective vaccines."

VACCINES IN CEREBRO-SPINAL MENINGITIS.

Much interest has been evinced in this country in this dread disease by the appearance of a widespread and quite fatal epidemic in many towns in Texas.

The applicability of vaccines in the treatment of this condition is still a moot question, for unfortunately, as many physicians have found out to their sorrow, the onset of cerebro-spinal meningitis is so sudden and the results of the infection so masked until they are beyond control, that to administer a vaccine in the treatment of this disease with the expectation of satisfactorily stimulating the immunizing response, would be practically useless. If such a response can be stimulated early—before the intoxication is so marked—then this method of treatment would be extremely valuable. So at present the widest field of usefulness for a vaccine made from the meningococcus is in prophylactic work.

The extensive epidemic of cerebro-spinal meningitis in Texas and surrounding country extending from the winter of 1911-12 to 1913 offered a good opportunity for studying the prophylactic value of meningococcus vaccine. Early in the epidemic I procured cultures obtained from lumbar punctures of cases in Houston, Texas. Vaccines were prepared, tested, and then applied for prophylactic

immunization. Through an extensive correspondence with physicians in the territory where the epidemic prevailed much information was gained concerning the advantages of prophylactic immunization. These physicians were advised to immunize at least every person who was exposed. No untoward effects from the use of the vaccine were noticed. From early in 1912 on through to 1914 many thousands of doses of meningococcus vaccine were supplied from my laboratories to Texas and surrounding territory and so far no report has reached me of a single case contracting the disease that received two or more prophylactic injections.

Meningococcus vaccine, as in the administration of typhoid vaccine for immunizing purposes, is given in three separate doses at intervals of five to seven days. From 250,000,000 to 500,000,000 killed germs are administered in the usual manner. The reaction, like that in anti-typhoid inoculations, may cause slight local pain and a passing malaise. If these conditions have all disappeared, the second dose of 500,000,000 to 750,000,000 is given between the fifth and seventh day. Usually the second dose causes a diminished reaction and sometimes no reaction at all. One week later a third dose of 1,000,000,000 completes the immunizing process.

Dr. Henry Martmer, Assistant State Health Cfficer and Bacteriologist of Texas, reports some of the results from prophylactic inoculations with meningococcus vaccine during the winter of 1912-1913 in the Bulletin of the Texas State Board of Health, and I will quote as follows:

"Those to whom the vaccine was administered included doctors and nurses attending cases of meningitis and members of families in homes where the disease existed. There were very few contacts who did not receive the prophylactic treatment. Many of the vaccinated were frequently exposed to meningitis. Of the entire number, about 3,500,

vaccinated in Austin and Manor, only a single one, an inmate of the lunatic asylum, developed the disease (in one of the wards for colored where there had been four cases). It is to be mentioned also that by far the greater number of the cases of meningitis in the city developed (among the unvaccinated) after a large majority of those vaccinated had received a part or all of the prophylactic treatment. Following the rapid invasion of the ranks of the Legislature there were no further cases of meningitis among the members of that body after a large majority of their number had received the second injection. None of the 1,000 or more vaccinated University students had meningitis.

"The blood of a number of those vaccinated was tested to find whether an immunity had been developed. In carrying out these tests we were fortunate enough to have had an opportunity, through the courtesy of local physicians, to get blood from meningitis cases to compare with blood of vaccinated cases and blood from a healthy person who had not been vaccinated. It was found that a rather high degree of immunity had been developed in nearly every case twelve days after the last injection of the treatment, and that three months later a slightly smaller per cent still showed evidence of a high degree of immunity."

Major Wadham (The Military Surgeon, August, 1913) was called to take charge of the sanitary conditions in a camp of refugees at Deckerville, Arkansas, as a result of floods caused by a break in the levee of the Mississippi, where epidemic cerebro-spinal meningitis appeared. Those having the disease were treated with Flexner's serum and the rest of the camp immunized with meningitis vaccine. The results from the vaccine are best given in the major's own language:

"As stated above, over 600 persons received the protective inoculation, and while it is impossible to draw any definite conclusions from this experience, the results are suggestive. The conditions existing in the community were ideal for the spread of the disease. There were several hundred people, mostly negroes, living in overcrowded and ill-ventilated box cars. Medical supplies and equipment were of the most primitive. None of the methods normally employed for controlling this disease, particularly

isolation and quarantine of contacts, could be employed. Yet the spread of the disease stopped suddenly and absolutely and I am informed no new case has since appeared in this community. It does not seem probable that cleanliness alone could produce this result. Yet cleanliness of the camp and vaccination of the people were the only means employed—in fact the only means that could be employed to combat the epidemic.

"The experience of Deckerville was most fortunate when contrasted with that of a neighboring town where two months before the disease had appeared. In the latter community the people were living under normal conditions. No prophylactic inoculations were made. There were a large number of cases in proportion to the total population with a high death rate, and stamping out of the disease was slow and difficult.

"The writer wishes to acknowledge the many courtesies received from Dr. Alexander, to whom he is indebted for the privilege of publishing these facts as well as that of observing the cases of meningitis, assisting in their treatment and in the vaccination of the people of the community."

The supplementary report made by Dr. J. H. Black, of Dallas, Texas, (Journal A. M. A., Dec. 12, 1914) is very interesting in that it shows conclusive experimental evidence of adequate antibody production for a considerable length of time from killed organism inoculations; in fact, a more pronounced immunity than developes by recovering from a meningococcus infection, and will quote as follows:

"In April, 1912, Dr. Abraham Sophian, then of the Research Laboratory of the New York Board of Health, and I conducted a series of experiments to determine, as well as laboratory methods will permit, the value of prophylactic vaccination against epidemic meningitis. Injections of meningococcic vaccine were made on ten medical students who volunteered for the work. The details of this work with the results obtained were reported in The Journal.*

"Eleven months later I repeated these experiments to

* Sophian, Abraham, and Black, J. H.; "Prophylactic Vaccination Against Epidemic Meningitis," The Journal, A. M. A., Aug. 17, 1912, p. 527.

determine what, if any, immunity could be demonstrated after the lapse of this time. Eight of the original ten vaccinated students were accessible. The technic used in the complement fixation studies was identical with that formerly reported. The results of this study were reported in The Journal.†

"With the effort to make this work as nearly complete as possible, I undertook in May, 1914, twelve and twenty-four months from the second and first examinations, respectively, a repetition of the complement fixation studies. Table 1 shows the results obtained. It will be seen that all but one of the seven students at hand gave decided fixation in a dilution of 1:20, this two years after the date of vaccination.

TABLE 1.—COMPLEMENT-FIXATION

Case No.	10	20	30	50	Control
1	++	++	—	—	—
2	+++	++	—	—	—
3	++	++	—	—	—
4	++	+	—	—	—
8	+++	++	—	—	—
9	+	—	—	—	—
10	++	++	—	—	—
Pos. con.	+++	+++	+++	++	—
Neg. con.	—	—	—	—	—

"Table 2 is a comparison of the fixation of each student at one month, one year and two years, respectively, after vaccination. The figures in each column refer to the highest dilution at which fixation was obtained.

TABLE 2.—COMPLEMENT-FIXATION

Case No.	1 Month	1 Year	2 Years
1	200	150	20
2	200	150	20
3	100	150	20
4	100	100	20
5	30	*	*
6	*	*	*
7	200	150	*
8	250	100	20
9	100	250	10
10	200	250	20

* Student not accessible.

† Black. J. H.; "Prophylactic," The Journal, A. M. A., April 26, 1913, p. 1289.

"While it is recognized that experimental vaccination of healthy individuals in the absence of an epidemic and the detection of immune bodies in their blood is an indirect way of proving its efficacy, and that the method must finally be judged by its clinical application, we feel that we are justified in drawing the following conclusions from these studies:

"1. Prophylactic vaccination produces a high degree of immunity in most cases, this immunity being demonstrable at the end of two years. It seems a justifiable conclusion that most persons prophylactically vaccinated may safely consider themselves immune for at least two years. Exceptions to this will, of course, be found.

"2. Some individuals may show an actual increase in immune bodies at the end of one year over those demonstrable soon after vaccination.

"3. Fixation occurred with the serum of the positive control who has recovered from meningitis, but this fixation did not reach as high dilutions as did that of some of those vaccinated. This has previously been found also in some others recovered from the disease.

"4. Experimental evidence warrants us in concluding that prophylactic vaccination is a measure of the greatest value in the control of epidemic meningitis."

Thomas and Ivy ("Applied Immunology," p. 300) point out that of 10,000 persons receiving full immunizing doses of meningococcus vaccine during epidemics of cerebro-spinal meningitis none contracted the disease. They quote Albright as saying that "meningo-bacterin is of as much value as a prophylactic in meningitis as typho-bacterin is in typhoid fever."

TREATMENT OF CEREBRO-SPINAL MENINGITIS.

The foregoing most conclusively shows the prophylactic value of meningococcus vaccine. From the pronounced immunizing responses that develop after prophylactic inoculations of meningococcus vaccine it is reasonable to suppose that similar antibody production would follow vaccine inoculations in cases of meningococcus cerebro-spinal

meningitis. That increased antibody production follows meningococcus inoculations in cases of cerebro-spinal meningitis is entirely probable, but in this disease the toxic symptoms are so pronounced and so dangerous that insufficient time is left to depend on antibody production under their antigenic influence and for that reason it is better to give the patient an immune serum which contains antibody previously prepared and ready for immunizing action; but meningococcus vaccine may be advantageously employed in conjunction with anti-meningococcus serum. There are many cases of meningitis in which improvement takes place after giving anti-meningococcus serum, and then remain stationary or relapse and get worse. In such cases meningococcus vaccine may be given to advantage in doses ranging from 200,000,000 to 500,000,000 or more, repeated at two to five-day intervals.

The serum treatment of epidemic meningitis is, of course, a little away from the scope of this book. However, it may be well to say that the tedious and persistent experiments of Dr. Simon Flexner and his assistants at the Rockefeller Institute in New York have given us a serum which is by far the most effective means of treatment as yet known. Its preparation is quite similar to that of other sera, as, for example, anti-diphtheritic serum and anti-tetanic serum. Horses are carefully and gradually immunized by increasing doses of meningococcus until finally an immense dose can be given with impunity. The serum constitutes the remedy, and the method of procedure is to withdraw 15 or 20 c.c. of spinal fluid directly from the patient and immediately substitute in its place the same or a slightly smaller volume of the curative serum. This neutralizes in a large degree the toxicity of the spinal fluid and permits the body to reassert itself.

In this connection it may be well to quote from a report by Passed Assistant Surgeon W. H. Frost, published in

Public Health Reports, No. 69: "The use of anti-meningococcus serum in the treatment of this disease may be now considered to have passed beyond the experimental stage and to have been established as a therapeutic measure of such well proven efficacy that its use becomes imperative. Now that the serum may be obtained readily upon the market in this country, it becomes the duty of those who undertake to treat cerebro-spinal meningitis to inform themselves as to the principles and methods involved in this therapy."

Further information on this subject may be secured from the annual reports of the Health Department of the City of Richmond, Va., for the year 1910, and from Ernest Levy's excellent article, "Serum Behandlung der Uebertragbaren Genickstarre," published in Klinisches Jahrbuch, June, 1911, Vol. XXV., pp. 121-272.

HODGKIN'S DISEASE.

It is now eighty-four years since Hodgkin reported a series of cases of the malady which takes its name from him as its discoverer. During all this time no treatment has been employed that had any material influence on the progress of the disease, until recently in a limited number of cases bacterial vaccines were employed. The results obtained therefrom is another striking evidence that killed organisms, when injected into healthy tissues, stimulate tissue cells for more antibody production than does the presence of live organisms in the infected area.

The disease was ascribed to various causes including malignancy. Struberg contended that it was due to some gram-positive non-acid-fast bacillus in smears prepared from the glands in a series of cases. This organism was believed by him to be the cause of the disease. Bunting and Yates in this country, and Negri and Mieremet abroad, isolated and cultivated an organism which conformed to the one described by Fraenkel and Much, in 1913.

Billings and Rosenow (Journal of the Amer, Med, Asso., Dec, 13, 1913, p. 2122) report the isolation and cultivation of a polymorphous diphtheroid bacillus corresponding to the organism described by others. The organism was grown on Loeffler's blood serum and other culture media, and after sufficient growth was secured a vaccine was prepared by the usual methods. Bacterial examination of the lymph-nodes in 12 cases showed the same bacillus in all of them. In some cases staphylococci were also found. Autogenous vaccines were employed in all but one case. The dose ranged from 5,000,000 to 100,000,000 organisms and inoculations were made at five to seven-day intervals. Four of the cases were too far advanced to render possible any results from the use of the vaccine. One case is reported as being well and the other as improving.

Drs. A. R. Hatcher and W. G. Lemon, of Wilmington, Kans. (Journal of the Amer. Med. Assn., Oct. 16, 1915) report an interesting case as follows:

History.—A retired farmer, aged 63, married, who had had rheumatism when a child, and occasional attacks of myalgia since, but no other illness. In the latter part of February, 1914, had what he described as a 'breaking out on the face.' A few days later he noticed swellings beneath the angles of the jaws and ears; these gradually increased in size, and in two or three weeks, swelling was noticeable in the axilla and groins. The tumor formations were never painful, tender or red. He rapidly became weak and emaciated, and complained of extreme nervousness.

Examination.—Tumor formations as shown in Figure 1 (illustration in the original not reproduced here) were present. The masses apparently consisted of enlarged discrete, non-adherent, painless, lymph nodes. The mucous membranes were pale. Physical examination otherwise was negative.

The urine was pale, amber, acid, specific gravity 1,008, albumin and sugar negative. Microscopically there were a few hyaline casts and amorphous urates. The red corpuscles in the blood numbered 3,200.00; hemoglobin, from 55 to 60; white blood cells, 7,200; ploymorphonuclears, 59; mono-nuclears, 41.

Treatment.—In June, 1914, one of the glands was taken from the neck and sent to Dr. F. W. Gaarde, of Chicago, for diagnosis and preparation of autogenous vaccine.

July 1, 1914, vaccine therapy was begun, consisting of subcutaneous injections twice a week for seven weeks. There were no severe reactions. The initial dose was 25,000,000; this was gradually increased to 2,000,000,000, and in addition to this the patient was given Roentgen-ray treatment every five days for eight weeks. He received six injections before there was any amelioration in the symptoms or the size of the glands. After this they gradually reduced to about two-thirds of their original size. August 27, he was taken ill with acute suppurative appendicitis. He was operated on, September 8, and an abscess was drained. The tubes were removed on the eighth day, and drainage ceased about the eighteenth. During this time there was an extremely rapid decrease in the size of the glands. With cessation of pus there was a corresponding slackening in the retrogression of the glands which did not cease entirely, but has continued until the present time.

Constitutionally, except for a dragging sensation at the site of the scar, the patient feels perfectly well, and is doing his own chore work on the farm.

The question arises as to what influence the pus infection had on the glands. There is no doubt that the toxins from infectious processes at times exercise a profound effect on newly formed tissue, as illustrated by the use of Coley's toxins in sarcoma. The fact, however, that the

glands were decreasing under the vaccine treatment, and continued to do so after the infection had cleared up, and that the results are identical with those of Billings and Rosenow, leads us to believe that while the appendicitis may have been a favoring influence, the main results were due to the vaccines.

Dr. D. C. Brockman (Chicago Medical Recorder, Nov. 1915) after giving an extensive review of Hodgkin's disease, concludes his paper by referring to the vaccine treatment as follows:

"A pure culture of the diphtheroid bacillus is obtained from the newly-developed nodes which are killed and injected in increasing doses till reaction is obtained. The early cases seem to respond readily to this treatment, but whether cures will be effected by it time alone will tell.

"In old chronic cases it seems necessary to make a vaccine from the oldest nodules which contain streptococcus as well as the specific bacillus, but thus far the improvement has not been so marked as in the earlier cases. All we are justified at this time in saying is that the results thus far are more encouraging than those obtained by any other line of treatment. Of course, besides the vaccine treatment, the X-ray should be used in full dosage; arsenic and iron, together with sunshine, fresh air and nutritious food, should be crowded to the limit.

"Every case treated by the vaccines should be closely observed and later reported, so that in time the value of the treatment may be determined."

VACCINES IN GOITER.

In my varied experiences with the use of bacterial vaccines I have frequently noticed that enlargements of the thyroid gland would subside simultaneously with improvement of the infection for which vaccine treatment was instituted. In such cases the question naturally arises whether the thyroid gland enlarges as a means of combating the toxic materials that are produced as a result of the infec-

tion in other parts of the body or whether the gland itself becomes infected.

Robert McCarrison (Lancet, Feb. 10, 1912) is of the opinion that the thyroid gland is Nature's method of combating certain toxins and that if additional toxins are to be combated as a result of an infection the thyroid gland enlarges from the additional necessary work.

Rosenow (Journal A. M. A., Sept. 12, 1914, p. 906) is of the opinion that goiter is due to an infection of the thyroid gland. He says:

"The etiologic role of infection in goiter is becoming more apparent; enlargement of the thyroid gland has been noted in various infections, particularly in rheumatism; and the peculiar distribution of endemic goiter, and other clinical facts, suggest that the cause of simple and exophthalmic goiter may be due to an infection. The symptoms and the enlargement of the gland, however, have usually been considered toxic in nature and not due to localization of the bacteria in the gland. No one, as far as I can learn, has isolated an organism from the thyroid in a series of cases. The fact that the same organism has been isolated from goiters in both dogs and man, and in the latter apparently in proportion to the degree of symptoms and from the blood, the absence of this organism in normal thyroid glands in dogs, the fact that it lives longer in the thyroid gland than in the kidney and other tissues of dogs following intravenous injection, and that goiter has appeared in two dogs after intravenous injection of this organism, suggest that goiter may be due not only to toxins produced in other regions of the body but to an actual localization in the gland of bacteria. Studies of the chief organism found show that it is probably closely related to the streptococcus group and this may explain why thyroid enlargement is observed commonly in rheumatism and in cases having foci of infection in which the predominating flora is streptococcal."

Billings (Journal A. M. A., Sept. 12, 1914, p. 901), in referring to the relation of thyroid enlargement and focal infections, says:

"None of these reporters mention the probability of the

thyroid enlargement and tenderness being due to the same rheumatic infectious agent of focal origin.

"These reports and the meager personal experience noted in the cases cited aroused the interest of the clinic as to the possibility of focal infection as a cause of goiter. The following case-reports are interesting and seem to show that there is an infectious type of goiter with and without symptoms of exophthalmic goiter, which seems to be of focal origin. The rapid subsidence of the goiter and the symptoms after removal of the foci of infection in the jaws and tonsils was a surprise. Bacteriologic examination of the tissues and alveolar pus revealed mainly streptococci. Autogenous vaccines were used with one exception in all the patients. No drug treatment with the exception of iron, for one, was used."

Enlarged thyroids are common in all kinds of chronic infections where the streptococcus is a prominent factor in the infection. This would include cases of pyorrhea and other mouth infections, tonsillitis, sinus infections, bronchitis, frequent attacks of colds, infections of the digestive tract, and rheumatisms. I have frequently found that when a person with an enlarged thyroid takes cold or some other localized infection, the gland is liable to become somewhat larger and tender on pressure during an attack. This would indicate that the thyroid gland becomes inflamed in all probability as the result of an infection in the gland.

I have found that if vaccines are employed in these cases, thyroid improvement will take place simultaneously with improvement of the localized infection. From this experience there is good reason to believe that if vaccines were regularly employed in the treatment of the more common infections hyperthyroidism would in a great measure be avoided.

BACILLUS PYOCYANEUS INFECTIONS.

Bacillus Pyocyaneus Infections are not of every-day occurence but are sufficiently often met to deserve con-

sideration. The organism is most frequently found as a secondary invader in chronic ulcers and more particularly in cases of chronic suppurative otitis media. In occasional instances it appears to be the principal infecting organism. Allen reports a case of hip-joint disease in which the organism was procured in pure culture six weeks after operation. There was much fever accompanied by other constitutional disturbances. This subsided promptly after using an autogenous vaccine and all the abscesses and sinuses healed except one quite small superficial one.

When the bacillus pyocyaneus is found as a secondary invader where other pus organisms are present, its pathogenic influence is not well established. Some observers contend that in such cases it simply acts as a scavenger while others attach some importance to it. I have used bacillus pyocyaneus vaccine without any results, especially in middle-ear cases. I find that by using vaccines for other organisms, local antiseptics usually will take care of the pyocyaneus infection.

In one case of chronic bronchitis associated with severe attacks of asthma I found almost a pure culture of bacillus pyocyaneus. A vaccine was prepared from the organism and doses of 100,000,000 combined with 30,000,000 streptococcus was given at weekly intervals. Improvement was observed after the third inoculation and after fourteen doses the patient was entirely well.

In one case of neuritis associated with some cystitis the bacillus pyocyaneus was found in the urine. A vaccine was prepared but no benefit was obtained from its administration.

A large variety of opinions exist as to the value of pyocyaneus vaccine. Some consider the vaccine of value while others think it is useless.

Dr. Nathaniel Gildersleeve (Journal A. M. A., July, 1911, p. 286) in an attempt to arrive at some definite conclusions,

made an extensive investigation with various strains of the organism both experimentally and clinically and concludes as follows:

"1. A marked increase in both the opsonic and agglutinative elements can be induced in the animal economy by the injection of vaccines as well as living organisms. Therefore, employment of vaccine in treatment of local pyocyaneus infections would appear rational.

"2. However, there is also a toxin produced by the organism under consideration, the action of which manifestly cannot be counteracted by the use of the medicine.

"3. Should one decide to employ vaccine in treating these infections, such vaccine must be prepared from the organism concerned in the individual infection under treatment, and never from strains that have been cultivated on artificial media for a number of generations. These organisms soon lose their virulence under artificial cultivation and at the same time, at least to a great extent, their power of conferring immunity.

"4. Bacteriolytic elements could not be demonstrated in vitro under either aerobic or anaerobic conditions.

"5. The phenomena appearing in the peritoneal cavity of guinea-pigs and rabbits, following the injection of the organisms, are apparently essentially agglutinative and opsonic (phagocytic) but little evidence presented to confirm the statement to the effect that there is an active bacteriolysis.

"6. Old toxic filtrates or extracts from the cells produce little or no increase in the agglutinative and opsonic functions; but the toxic filtrates do produce a high degree of immunity against such filtrates."

CHOLERA, PLAGUE AND MALTA FEVER.

Cholera is a disease in which dangerous symptoms develop so rapidly from infection by the cholera vibrio that therapeutic vaccine inoculations are of questionable value. Prophylactic inoculations of cholera vaccine, however, have proven of great value.

Haffkine advised the use of a vaccine prepared from

attenuated live organisms. The attenuation consisted in growing the cholera vibrio on ordinary laboratory culture media at a temperature sufficient to retard their growth to a minimum and then subculturing this attenuated organism to procure stock for the vaccine.

Later experience, however, has demonstrated that a vaccine of killed organisms serves better for prophylactic immunization. What is true of the cholera vibrio is equally true of the plague and malta fever organisms.

The work of Castellani along this line of immunization is exceptionally interesting and was reported in the Lancet, November 27, 1915, as follows:

"A paper on 'Combined Vaccinations,' by Dr. Aldo Castellani, formerly of Colombo, but now professor of tropical medicine in the University of Naples, who has been recently working in the Serbian military hospitals, was read at the November meeting of the Society of Tropical Medicine and Hygiene. The following is a short summary of the conclusions of the paper. Professor Castellani thinks he is justified in saying that the preparation of combined vaccines is based on the experimental work which he carried out in 1901-1902 in Professor Kruse's Institute, when he demonstrated that in animals inoculated with two or three species of bacteria—provided a sufficient minimum quantity was given—agglutinins and immune bodies for all the germs were elaborated, the amount of agglutinins and immune bodies elaborated for each germ being nearly the same as in control animals respectively inoculated with only one species. He has prepared and used the following vaccines:

"1. Typhoid plus paratyphoid A and paratyphoid B.

"2. Typhoid plus paratyphoid A, paratyphoid B and cholera.

"3. Typhoid plus Malta fever.

"4. Typhoid plus paratyphoid A, paratyphoid B and Malta fever.

"5. Typhoid plus paratyphoid A, paratyphoid B, cholera and Malta fever.

"6. Typhoid plus paratyphoid A, paratyphoid B, B. asiaticus, and B. columbensis.

"7. Typhoid plus paratyphoid A, paratyphoid B, B. asiaticus, B. columbensis and Malta fever.

"8. Typhoid plus paratyphoid A, paratyphoid B, dysentery Kruse-Shiga, dysentery Flexner, dysentery Hys Y, dysentery Flexner-like No. 1 and dysentery Flexner-like No. 2.

"9. Cholera plus plague.

"10. Cholera plus plague, typhoid, paratyphoid A and paratyphoid B.

"11. Cholera plus plague, typhoid, paratyphoid A, paratyphoid B and Malta fever.

"The inoculation of the above vaccines in man is harmless; the reaction is not severe, with the exception of those containing plague, but even simple plague mono-vaccines give generally a severe reaction. The combined vaccines Professor Castellani is now using consist of carbolized emulsions of agar cultures in normal salt solution without heating. These emulsions seem to give a less painful reaction than broth cultures killed by heat. The presence of 0.5 per cent carbolic acid is sufficient to kill the germs. The individuals inoculated with those of the above-mentioned vaccines, which contain two or three or four species of bacteria, generally produce agglutinins for each species of bacteria. The amount of each species is not much less than that observed in control individuals inoculated with simple 'one disease' vaccines. Of the vaccines containing more than four species, some, as for instance the plague plus cholera, typhoid, paratyphoid A and paratyphoid B vaccine, seem to give good results; others are not so satisfactory, protective substances developing only for two or three or four species and suddenly disappearing. The combined vaccines which Professor Castellani has found most useful from a practical point of view are the typhoid plus paratyphoid A and paratyphoid B vaccine, and the tetravaccine typhoid plus paratyphoid A, paratyphoid B and cholera. The latter vaccine has been prepared in Serbia on a large scale by himself, with the assistance of Dr. Mendelson and Dr. Borvic; it was officially adopted by the American Red Cross Sanitary Commission and by the Serbian Government, and more than 170,000 men were inoculated with good result.

Finally, it may be stated that these combined vaccines, when efficient, are of practical advantage, saving a great deal of time and rendering possible a contemporaneous vaccination for several different maladies.—Annotations."

SMALLPOX.

The etiologic organism in smallpox has never been isolated, so a smallpox bacterin for the treatment of the disease is not available. From the course of the disease, however, it is quite apparent that the pus cocci are an important factor of the disease. In the more severe cases of smallpox the fever continues at its high level until the eruption on the skin appears. About the time the eruption has developed into the vesicular stage the temperature declines and the patient feels better. These vesicles soon develop into pustules, when the temperature again begins to rise and it is during this stage of the disease that the most serious symptoms usually develop. Bacterial examination of the pustules shows streptococci and staphylococci. From this it is clear that the toxic symptoms during this stage are mainly due to infections by these organisms, as secondary invaders. The ravages of these pus organisms not only endanger the life of the patient, but they are mainly responsible for the extensive pitting that so often follows smallpox. Here a combined streptococcus-staphylococcus vaccine will serve a good purpose. By immunizing the patient to these organisms the pustular eruption will naturally become less extensive, with corresponding benefit to the patient.

MEASLES.

To my knowledge no vaccine has been prepared for the treatment of measles. In the treatment of measles, however, we find that pneumonia or broncho-pneumonia are the most dangerous complicating factors of the disease. It has never been demonstrated that the pneumonia in these

cases is due to the infecting organism which is responsible for the measles. On the other hand, pneumococci, streptococci, and staphylococci are regularly found in the sputum of patients suffering with measles complicated by a pneumonia. For this reason it is fair to assume that these organisms are responsible for the pneumonia or broncho-pneumonia as secondary invaders.

In my experience a combined pneumococcus, streptococcus, staphylococcus vaccine has given good results in pulmonary complications associated with measles. The dosage and intervals between inoculations are the same as in other cases of pneumonia and broncho-pneumonia.

PALLIATIVE TREATMENT OF CANCER WITH VACCINE.

Since we have no specific for the treatment of cancer necessarily our efforts must be directed toward giving such cases as much relief as possible. Surgery, X-Ray, and Radium have their place, and by these means much can be accomplished but every physician sees cases that are beyond any curative measures where the problem of giving relief is of greatest importance.

Infections by pyogenic organisms are always associated with advanced cancers and much of the pain in cancerous growth is due to the ravages of these infecting organisms. There is nothing more striking in vaccine therepy than the relief from pain as immunization develops in the course of an infection. I have found that by employing vaccines in cancer cases, pain, due to infections, can be almost entirely eliminated.

When employing vaccines for this purpose it is necessary to select a vaccine containing the organisms that prevail in the infections usually present in the part of the body where the cancer is located. In cancers of the mouth and throat the same vaccine should be employed that is used

in mouth and throat infections. If the cancer involves the abdominal viscera, rectum, or pelvic organs, the vaccine should contain the organisms that prevail in infections of these organs.

As a rule in cancers of the mouth and throat a combined vaccine containing streptococci, pneumococci, staphylococci and the micrococcus catarrhalis serves the purpose. In cancers of the abdominal viscera and pelvic organs a combined vaccine containing colon bacilli, streptococci, pneumococci, and staphylococci should be employed. The dosage and intervals between inoculations is the same as when employing these vaccines in chronic infections.

CHAPTER XXI.

TUBERCLE INFECTIONS.

General Considerations.

Infections by the Tubercle Bacillus are destructive in that they start insiduously, develop slowly and usually run a prolonged course.

Persistency, rather than severity of the infection, is a characteristic early symptom. Any localized infection that progresses slowly but persistently should be considered sufficiently characteristic to demand a careful bacterial or tuberculin diagnosis by the Von Pirquet, Wolff-Eisner-Calmette, or other tuberculin tests.

Any part of the body is subject to infection by the tubercle bacillus and from the standpoint of immuno-therapy the treatment is necessarily the same regardless as to the part of the body that is involved. Mixed infections in which the ordinary pyogenic organisms grow side by side with the tubercle bacillus are the rule. In fact these pyogenic organisms are most important etiologic and pathogenic factors in tubercle infections. In pulmonary tuberculosis the tubercle infection is usually preceded by a "cold," bronchitis, broncho-pneumonia, or pneumonia. Whether in such cases a dormant tubercle infection existed prior to the acute infection by the organisms responsible for the bronchitis or pneumonia, and then becomes active from the resulting lowered resistance of the lung tissues, or whether these organisms paved the way for a subsequent tubercle infection is not so readily determined. No doubt both conditions prevail. What is true of pulmonary tuberculosis is equally true in most other localized tubercle infections. The fact that pyogenic organisms are responsible for much of the destruction in tubercle infections and that these organisms greatly facilitate the growth of the tubercle bacillus is now well established.

The pyogenic organisms complicating tubercle infections are usually the same as those most frequently found in the common infections of the various parts of the body. In pulmonary tuberculosis the mixed infection as a rule consists of pneumococci, streptococci, staphylococci, the micrococcus catarrhalis, and after the prevalence of influenza infections, the influenza bacillus. In tuberculosis of the abdominal viscera and urinary tract we have the colon bacillus, staphylococcus, streptococcus and pneumococcus as the complicating organisms in the mixed infection. Tubercular joint infections are usually complicated by the staphylococcus and not infrequently the streptococcus. Tubercular infections of the nose and throat are complicated by the same organisms that prevail in pulmonary tuberculosis.

In following out specific therapy in tubercle infections the importance of also instituting immunizing measures to take care of the mixed infection is too often disregarded, and no doubt accounts for many of the failures from the use of remedies that are specifically directed towards the elimination of the tubercle infection. To eliminate the tubercle bacilli from an infected area it is necessary to establish an unfavorable condition for their growth, and this can only be accomplished by also making conditions unfavorable for the growth of the organisms causing the mixed infection.

The treatment of tuberculosis by the immunizing method has received an unusual amount of continuous attention from the time that Koch brought out his tuberculin in 1890 until now. I can well remember with what anticipations I employed Koch's tuberculin in those early days, only to be dissappointed after having given the treatment a trial. Sir A. E. Wright deserves the credit for having placed therapeutic immunization in tubercle infections on a scientific basis. By means of his opsonic index he demonstrated that tuberculins were employed in entirely too large dosage to obtain immunizing responses and that the trouble was not so much in the remedy as in the way it had been employed.

Meantime anti-tubercle serums were developed but none of them possessed marked therapeutic immunizing properties. Special attention was also directed towards preparing tuberculins or tubercle antigens for therapeutic inoculations with the idea of eliminating the toxic materials and retaining the portion that stimulates antibody production. Tuberculinum purum or Endotin is prominent among this class of preparations. Tuberculins prepared by different methods, such as Bullion Filtrate (B. F.) Tuberculine Residue (T. R.), and other similar preparations have been extensively employed. Bacillin Emulsion (B. E.) is prepared by finely grinding the tubercle bacillus and making a suspension. This preparation has been preferred by many because it contains all the constituents of the tubercle bacillus and for that reason is supposed to possess greater antigenic properties to stimulate antibody production.

I have employed these various preparations with varying results. As a whole there can be no doubt but that tuberculins are of great value in stimulating antibody formation when employed so as to avoid reactions and especially so when carefully used in conjunction with bacterial vaccines to combat the mixed infections that are usually present.

The Non-Virulent Tubercle Bacillus.

Three years ago I procured a culture of a non-virulent tubercle bacillus which is so attenuated that inoculations of large numbers of the live organisms are tolerated by guinea pigs and other animals without ill effects.

The organisms grow freely on ordinary solid culture media and produce an almost pure white growth, in appearance very similar to the growth from a staphylococcus albus and grows about as freely at room temperature as in an incubator. On liquid culture media the organism does not grow as freely as the human variety. This tubercle bacillus is acid fast and in microscopic appearance like the

human variety. That this organism is a true tubercle bacillus has been demonstrated by complement deviation and other immunizing tests.

The prominent antigenic properties of this non-virulent tubercle bacillus, when employed as a vaccine by injecting the killed organism, towards human tubercle infections is well illustrated by animal experimentation as shown by complement fixation, opsonic index.

Complement deviation tests are now recognized as most delicate in determining the presence of a certain infection. For example: A positive Wasserman shows by complement fixation that certain antibodies that have developed as a result of a syphilitic infection are present in the blood. A positive complement fixation in a case of gonorrheal infection shows that a gonococcus infection with enough tissue involvement exists to elaborate sufficient gonococcus antibody so it may be found in the blood. The presence of a tubercle infection may be determined by the same method.

Furthermore, it has been demonstrated that by injecting killed organisms under the skin, a positive complement fixation or deviation will take place to the organisms thus injected, showing that antibodies are developed. If killed organisms of one type are injected and complement fixation of the blood serum becomes positive to an organism of another type we have certain proof that the killed organism when injected possesses the faculty of stimulating antibody production to the other organism. What is true with regard to complement fixation also holds good with opsonic and other immunizing actions.

For the purpose of determining the immunizing properties of this non-virulent tubercle bacillus when the killed organisms are injected under the skin towards human tubercle infections the following animal experiments were instituted.

COMPLEMENT FIXATION TESTS.

An antigen was prepared by grinding fresh human tubercle bacilli and suspending them in normal salt solution in a sterile glass stoppered bottle in which were placed some sterile glass beads, then incubated for five days. To break up the suspension thoroughly the bottle was vigorously shaken twice daily. The emulsion of the disintegrated bacteria was then passed through a Chamberland filter and the filtrate tested for sterility.

Table No. 1 shows the results of complement fixation tests on six guinea pigs. The blood of these pigs was tested and found negative to tubercle reactions before they were injected with the non-virulent tubercle vaccine. It will be noted by examining the table that antibodies to the human tubercle bacillus were developed soon after the vaccine inoculations.

TABLE No. 1.

Guinea Pig	Relation to Injection	Degree of Fixation
No. 1	48 hours after 1st	++
1	4 days after 1st	—
2	48 hours after 1st	+
2	4 days after 1st	—
3	48 hours after 1st	+
3	4 days after 1st	+
3	8 days after 1st	++
4	48 hours after 1st	+
4	4 days after 1st	+-+
4	8 days after 1st	+-+
5	48 hours after 1st	+
5	72 hours after 1st	+-+
5	9 days after 1st	+
6	24 hours after 1st of 350,000	—
6	72 hours after 1st of 350,000	+
6	48 hours after 2d of 750,000	—
6	72 hours after 2d of 750,000	++
6	1/200 hours after 2d of 750,000 ...	+
6	9 days after 2d of 750,000	+

In making this test advantage is taken of the known fact that antigens will combine with antibody in the presence of complement while the complement is being consumed to the extent that antigen and antibody combine. To carry out the test the blood serum to be tested is heated in a water bath to 56C. for half an hour. This destroys or inactivates the complement normally contained in the serum. A given amount of tubercle extract or antigen and just enough complement are then added to a given amount of the inactivated serum to completely dissolve a certain amount of sheep blood corpuscles suspended in normal salt solution in the presence of sheep blood amboceptor. We then have a serum standardized in complement mixed with the tubercle antigen in the presence of a certain amount of sheep blood corpuscles suspended in, usually 1 C. C. of normal salt solution. A control in every respect identical except that no tubercle antigen is added, is also prepared. The tubes are then incubated for half an hour. If specific antibody is present in the blood serum it will combine with the tubercle antigen that has been added, and some or all of the complement in the tube that contains the tubercle antigen will be consumed. If now sheep corpuscle amboceptor, a substance that will dissolve sheeps corpuscles in the presence of complement, is added, and incubated for twenty minutes it will be found that the corpuscles in the tube containing no tubercle antigen will be disolved while the corpuscles in the other tube will remain whole. In other words, the complement in the tube containing the tubercle antigen combines with the tubercle antibody present in the serum under examination, and consequently there is no complement left to link the sheep corpuscles with the sheep amboceptor to dissolve them. By employing the serum in different dilutions an approximate idea may be

obtained by this method as to the amount of specific antibody that is present in the blood.

Table No. 2 shows that the amount of antibody produced bears a certain relation to the size of the dose of non-virulent tubercle vaccine given and the time the experiment was made after the vaccine inoculation.

TABLE No. 2

Guinea Pig	Dose	Relation to Injection	Fixation
No. 1	350,000	48 hours after 1st	+
1	.....	4 days after 1st	...
2	10,000,000	48 hours after 1st	++
2	.....	4 days after 1st	...
3	350,000	48 hours after 1st	+
3	.....	4 days after 1st	...
4	350,000	48 hours after 1st	+
4	.....	4 days after 1st	—+
4	.....	8 days after 1st	++
4	.....	2 weeks after 1st	...
5	10,000,000	48 hours after 1st	+
5	.....	72 hours after 1st	++
5	.....	9 days after 1st	+
6	350,000	24 hours after 1st	...
6	.....	72 hours after 1st	—+
6	.....	4 days after 1st	...
6	750,000	72 hours after 1st	++
6	.....	9 days after 1st	+

A series of experiments to determine the immunizing influence of killed suspensions of this non-virulent tubercle bacillus were also conducted by the Chicago Medical Research Laboratories under the direction of Dr. B. Gruskin and his associate, Frank Challis.

Ten guinea pigs were employed. Each pig was weighed and inoculated with Non-virulent tubercle vaccine in doses that would correspond to 250,000,000, 500,000,000, and 1,-

000,000,000 organisms given to man weighing 150 lbs. as compared with the weight of the pig. Inoculations were made at seven day intervals and the blood regularly examined for complement fixation and opsonic index to the human tubercle bacillus.

An examination of the charts will show a uniformity in antibody production soon after the inoculations of the non-virulent tubercle vaccine. In two pigs, No. 3 and No. 9 no complement fixation developed but it will be observed that these pigs lost in weight during the experiment. This was in all probability due to the necessary frequent bleeding of the pigs from the heart which frequently injures the heart.

The following is a complete reproduction of the charts, including Dr. Gruskin's remarks:

"The control serum used in all the following experiments consisted of the blood serum of four normal guinea pigs. The same pigs were used throughout the entire work.

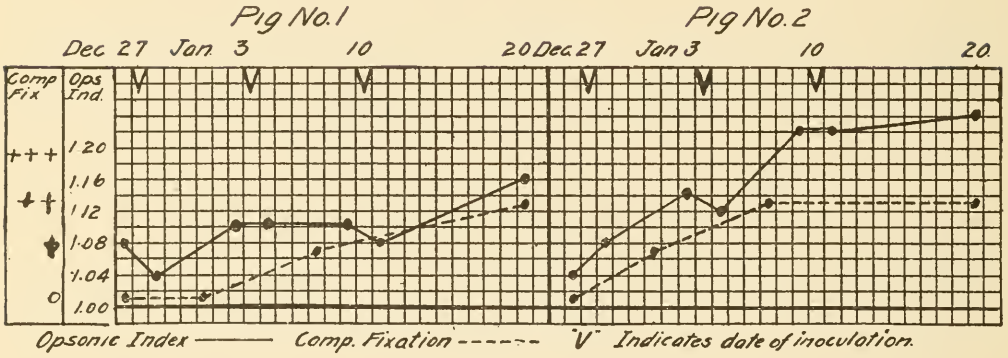
"The blood for opsonic indexes was obtained by clipping the margin of the ear—allowing it to flow into a Wright's capsule, all experiments were completed the same day that the blood was obtained.

"The bacterial emulsion was made with bacilli recently isolated from sputum—an emulsion made using Wright's technique.

"Except in pigs Nos. 3, 7 and 9 there was no change in temperature following the injections.

"In Nos. 3 and 9 a raise of 1 -1.5 was noticed, following each injection, and in No. 7 following the first injection only.

"Blood for complement fixation was obtained direct from the heart."



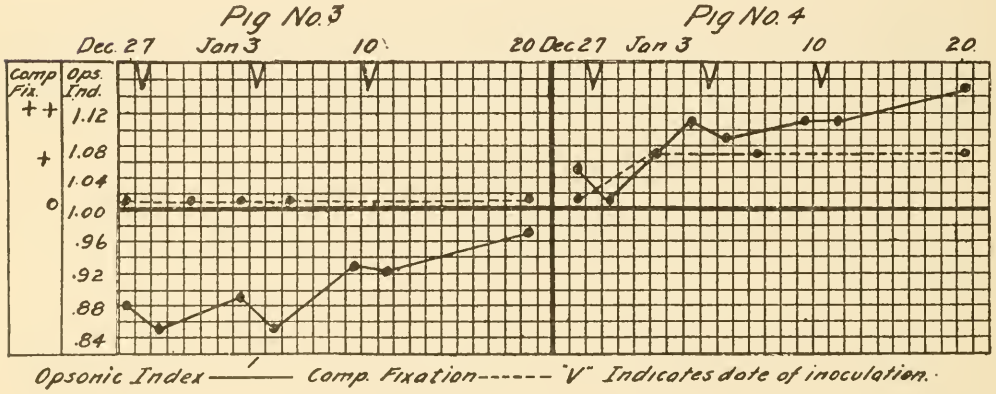
PIG No. 1
Weight at beginning of experiment. 400 grams
Weight at end of experiment. . . . . 400 grams
Inoculation with tuberculin. . Sherman's

	Non-Toxic
Dose No. 1	1.6 million
Dose No. 2	3.2 million
Dose No. 3	6.4 million

PIG No. 2
Weight at beginning of experiment. 450 grams
Weight at end of experiment. . . . . 470 grams
Inoculation with tuberculin. . Sherman's

	Non-Toxic
Dose No. 1	1.8 million
Dose No. 2	3.6 million
Dose No. 3	7.2 million

Serum of this pig showed marked agglutinating power for the Tubercle Bacillus.

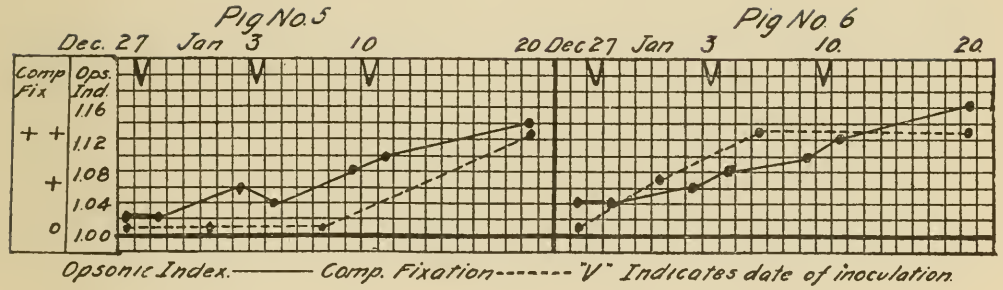


PIG No. 3
Weight at beginning of experiment. 300 grams
Weight at end of experiment. . . . . 280 grams
Inoculation with tuberculin. . Sherman's

	Non-Toxic
Dose No. 1	1.2 million
Dose No. 2	2.4 million
Dose No. 3	4.8 million

PIG No. 4
Weight at beginning of experiment. 500 grams
Weight at end of experiment. . . . . 506 grams
Inoculation with tuberculin. . Sherman's

	Non-Toxic
Dose No. 1	2.0 million
Dose No. 2	4.0 million
Dose No. 3	8.0 million



PIG No. 5

Weight at beginning of experiment. 500 grams
Weight at end of experiment. . . . . 500 grams
Inoculation with tuberculin. . Sherman's

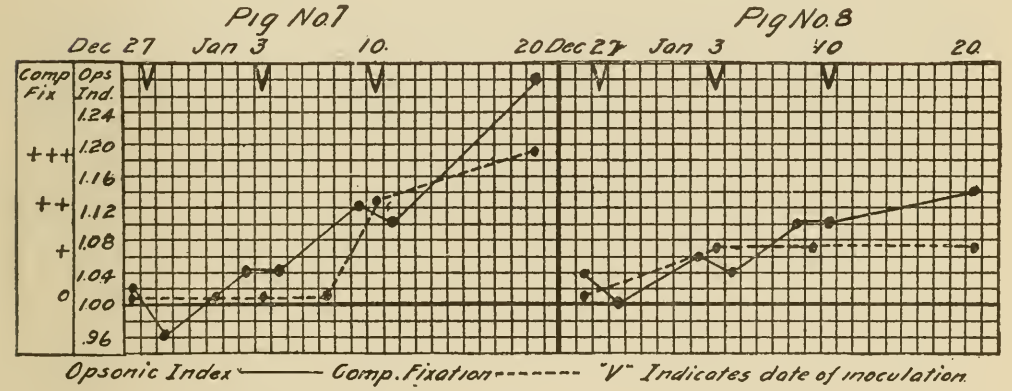
	Non-Toxic
Dose No. 1	2.0 million
Dose No. 2	4.0 million
Dose No. 3	8.0 million

PIG No. 6

Weight at beginning of experiment. 400 grams
Weight at end of experiment. . . . . 410 grams
Inoculation with tuberculin. . Sherman's

	Non-Toxic
Dose No. 1	1.6 million
Dose No. 2	3.2 million
Dose No. 3	6.4 million

Serum of this pig developed marked agglutinating properties for the Tubercle Bacillus.



PIG No. 7

Weight of pig before experiment. . . 300 grams
Weight of pig after experiment. . . . 280 grams
Inoculation with tuberculin. . Sherman's

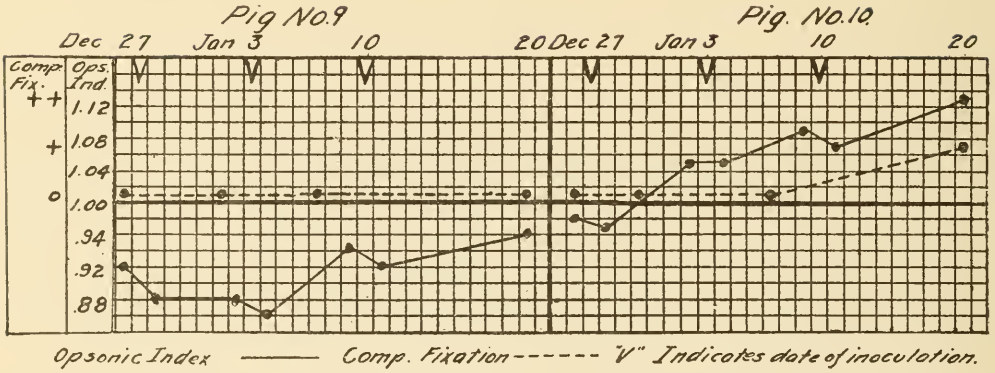
	Non-Toxic
Dose No. 1	1.2 million
Dose No. 2	2.4 million
Dose No. 3	4.8 million

Serum of this pig showed marked power of agglutinating the Tubercle Bacilli.

PIG No. 8

Weight of pig before experiment. . . 600 grams
Weight of pig after experiment. . . . 620 grams
Inoculation with tuberculin. . Sherman's

	Non-Toxic
Dose No. 1	2.4 million
Dose No. 2	4.8 million
Dose No. 3	9.6 million



PIG No. 9

Weight before experiment.....400 grams
Weight after experiment.....325 grams
Inoculation with tuberculin..Sherman's Non-Toxic

Dose No. 1.....1.6 million
Dose No. 2.....3.2 million
Dose No. 3.....7.4 million

PIG No. 10

Weight before experiment.....450 grams
Weight after experiment.....450 grams
Inoculation with tuberculin..Sherman's Non-Toxic

Dose No. 1.....1.8 million
Dose No. 2.....3.6 million
Dose No. 3.....7.2 million

THE NON-VIRULENT T. B. VACCINE.

Vaccines prepared from this non-virulent tubercle bacillus have, in my experience, given much better therapeutic results than tuberculins prepared from virulent human tubercle bacilli. The distinct advantage in employing a vaccine prepared from this non-virulent organism is that marked focal reactions that aggravate a localized tubercle infection or a prolonged negative phase does not follow its use, while at the same time marked immunizing responses develop.

From its non-toxic character this vaccine may be employed in advanced as well as incipient cases of tuberculosis. The best results are secured when treatment is started early. Tissues once destroyed cannot be replaced. To avoid extensive tissue involvement, therapeutic immunization should be instituted early and to do this an early diagnosis is most important.

In the treatment of tubercle infections we have incipient, moderately advanced and advanced cases to deal with. Like all other infections amenable to immuno-therapy

early treatment is most important to obtain the best results. As a rule incipient tubercular infections do well under hygienic treatment and in so far as improved hygienic conditions are always instituted in conjunction with the vaccine treatment it is often difficult to determine to what extent the vaccine treatment is responsible for the improved condition, but when the improvement is marked and soon follows the vaccine inoculations the benefit is rightly ascribed to the vaccine.

Mixed infections by the common pyogenic organisms being common or liable to become a factor in tubercle infections it is advisable to employ mixed vaccine containing the pneumococcus, streptococcus, and staphylococcus as a routine in conjunction with the tubercle vaccine.

In tuberculosis of the urinary tract, pelvic organs, or abdominal viscera the colon bacillus should be included.

In cases of pulmonary tuberculosis it is advisable to also include the other organisms usually found in infections of the respiratory tract or such organisms as a sputum examination would reveal.

In the preparation of bacterial suspensions for immunizing purposes it is important that the organisms in the suspension should conform as nearly as possible to the requirements of natural immunizing processes. For this reason, it has been found of advantage to inject the entire germ when employing vaccines prepared from the usual pyogenic or other organisms, because it requires some time for tissue cells to disintegrate the entire germ and it is during this disintegrating process that the immunizing mechanism is developed, whereas when disintegrated liquid germ substances are injected a certain sudden toxic reaction follows which is not necessarily immunizing in character. With the tubercle bacillus, however, we find that on account of its construction with a waxy or resisting fatty covering, when the entire organism is injected, tissue cells

in some instances are not capable of disintegrating the organisms and, in time, this may result in the formation of a sterile abscess. So, in the preparation of the non-virulent tubercle bacillus vaccine, we have taken advantage of this situation by partially grinding the organism with a specially devised grinder. This provides the advantage of injecting entire germ particles while the germs are sufficiently broken up so the tissue cells can take care of them and thus avoid the development of sterile abscesses.

Reactions from inoculations of the non-virulent tubercle bacillus vaccine vary greatly, in some cases large initial doses are tolerated without producing visible disturbance while in others much smaller doses cause considerable reaction, but these reactions are of short duration, and soon become less marked under increasing dosage. From experience we find it advisable to start treatment with 100,000,000 organisms as an initial dose. If a material reaction develops as shown by inflammatory infiltration at the site of injection, a rise of temperature attributable to the vaccine or a general malaise, the dose should not be materially increased until enough resistance has developed to tolerate the vaccine. The dose may then be gradually increased as indicated by the reactions and the progress made by the patient. When no material reaction follows the injection the dose may be increased by 100,000,000 or 200,000,000 at each subsequent inoculation until a dose of 1,000,000,000 organisms is reached, and in some cases even twice this amount is given. Inoculations are usually made at weekly intervals. To avoid conflicting reactions the mixed vaccine should not be given at the same time with the non-virulent tubercle bacillus vaccine. This vaccine should always be given three or four days later and in guaging the dose the same rules apply as when these vaccines are employed in the ordinary infections by these organisms. By this means the patient receives one dose of

each vaccine each week. Some doctors give the non-virulent T. B. vaccine at three or four day intervals with good results.

This general rule applies to the use of the non-virulent tubercle vaccine in pulmonary cases, tubercular arthritis, adenitis, iritis, nephritis, lupus or tubercle infections of any other part of the body.

In the early stages of tubercle infection I have found uniform good results from this combined vaccine treatment and especially so if accompanied by the recognized hygienic measures such as fresh air, nutritious food, proper rest, etc.

Good results are also procured in moderately advanced cases of which the following are a fair illustration.

Mr. R., age 25, student attending State University, weight 136 pounds. No tuberculosis in family to patient's knowledge. On February 22 patient complained of tiring easily, some pain in chest with dry, hacking cough which had been coming on for four months. Up to this time no fever was observed. Bacterial examination of sputum revealed tubercle bacilli averaging four to the field and among ordinary piogenic organisms the influenza bacillus was also found. A few days later an acute tonsillitis developed in conjunction with the influenza bacillus infection which caused considerable fever, and made the patient sufficiently ill to be confined to bed for over a week. With the aid of a mixed vaccine, containing the influenza bacillus, this acute illness soon subsided. Active treatment for the tuberculosis was undertaken at once, starting with small doses of tuberculinum purum, given at four-day intervals and gradually increasing the dose, the mixed vaccine containing the influenza bacillus being continued. Rest, fresh air, and other favorable hygienic conditions were instituted and two intravenous injections of an iron solution were given as a blood.tonic. Flouroscope examination by Dr. A. C. Huegli, on

March 12, and physical examination showed lung involvement of upper right lobe, principally under the scapula. General improvement from the influenza infection was observed, but the cough persisted and the sputum continued to have many tubercle bacilli.

On April 13, 1913, the first inoculation of 100,000,000 non-virulent tubercle vaccine was given with no reaction, but claimed he felt better after it. On April 18, 250,000,000 of the same vaccine was given followed by a marked local reaction at the point of inoculation and a rise of temperature of 100 2/5° F. There was also a focal reaction as shown by an increased amount of sputum expectorated which contained more tubercle bacilli than previous specimens. April 24, 300,000,000 of the same vaccine. No reaction after this inoculation. Amount of sputum, number of tubercle bacilli and cough becoming less. April 29, 500,000,000; slight reaction. Patient feeling much better, cough almost gone and tubercle bacilli comparatively few. After this, inoculations were made at about weekly intervals, increasing the dose from 500,000,000 to 750,000,000. Mixed vaccines to meet pyogenic infections and especially for a chronic catarrhal condition of the nose, were also given in conjunction with the vaccine. One week of this time was spent in a sanitarium, three weeks on a farm, and three weeks at a private summer cottage at St. Clair Flats. His cough is entirely gone, he has gained twenty-four pounds, fifteen pounds more than his normal weight, in less than three month's time. He has to all appearance entirely recovered.

He being engaged to get married, it was feared that the young lady might have become infected, although she appeared entirely well with the exception of a few enlarged lymphatic glands in her neck that had been there for several years. Treatment for prophylactic immunization was begun on February 28 by giving small, increasing doses of

tuberculinum purum at four-day intervals. A distinct local reaction with tenderness was observed in the enlarged lymphatic glands accompanied by a tired feeling after each inoculation. After giving five inoculations the treatment was discontinued. While feeling entirely well and working every day at bookkeeping, the reaction obtained from the tuberculin inoculations pointed towards a tubercle infection. After discontinuing these inoculations, the patient was advised to take her temperature daily, once in the morning and three times in the afternoon. Two weeks' record showed a constant afternoon rise ranging from 99° to nearly 100° without having any feverish or ill feeling.

On April 20, 1913, I gave her 25,000,000 non-virulent T. B. vaccine into the subcutaneous tissue of the arm. A marked local inflammatory reaction followed with the temperature going to 102 2/5° F. In four days the temperature became normal and remained normal. Two more inoculations of 25,000,000 were repeated at weekly intervals, each successive treatment showing less local reaction. The fourth inoculation of 45,000,000 was given 10 days later with no reaction. With the fifth inoculation of 100,000,000 no local reaction was observed, but temperature reaction followed, reached 99 2/5° every afternoon for five days with some tenderness in the lymphatic glands of the neck, but they have diminished to half their former size. The patient was allowed to continue at work, so the return of the temperature to normal could not be attributed to rest. Vaccine inoculations were continued for two months at weekly intervals. At the end of this time she felt entirely well and the enlarged lymphatic glands had practically disappeared.

In the fall of the same year the young folks got married. They are now the happy parents of a fine healthy boy nearly two years old.

Mr. K., aged 35, cigar maker, had been troubled with a cough for six months which was steadily growing worse.

He had always been thin but was losing in weight. His temperature ranged from subnormal to 101. He had not quit working but felt tired and unable to work. Sputum examination showed tubercle bacilli averaging five to a field. Rest in bed at an open window with an abundance of raw eggs and milk with other wholesome food was instituted. Vaccine treatment was started at once by giving non-virulent T. B. Vaccine and a mixed vaccine containing pneumococcus, streptococcus, staphylococcus and micrococcus catarrhalis alternately each at weekly intervals. There was but slight reaction from the tubercle vaccine so the dose was rapidly increased from 100,000,000 to 700,000,000 within six treatments. The mixed vaccine was also increased to the usual full sized dose by this time. He soon developed a good appetite with an equally good digestion. At the end of six weeks treatment he had gained thirty pounds in weight, his cough was gone and no more tubercle bacilli were found in his sputum. I continued vaccine inoculations for a time at weekly intervals then two or three weeks apart for three more months. It is now over two years since treatment was discontinued with no return of pulmonary symptoms.

Mr. W., a draftsman was suffering with a laryngitis which had been steadily growing worse for over a month. His voice was greatly interfered with, usually talking in a whisper. There was no bronchitis or lung involvement. Bacterial examination of throat cultures and sputum showed the usual pyogenic organisms but no tubercle bacilli were found. Vaccine treatment for the pyogenic organisms gave only partial relief after a four weeks trial. A complement fixation test for tubercle infection proved positive. Non-virulent T. B. vaccine was then given alternately with the mixed vaccine. Marked improvement was soon observed after giving the T. B. Vaccine and after three months treatment his voice had cleared up and the tender-

ness in the larynx was gone. It is now nearly two years since vaccine treatment was discontinued with no return of the symptoms.

Treatment in advanced cases at best can only be palliative and this is particularly true of advanced pulmonary tuberculosis. Such cases are often abandoned as far as immuno-therapy is concerned. This is a great mistake. Even as a palliative measure to relieve pain, excessive coughing and other disagreeable symptoms vaccine inoculations will accomplish more with more lasting effects than drugs. A low resistance in the presence of an infection is always associated with much suffering and as immunization develops this suffering becomes less. This also holds good even in advanced infections and is especially noticeable in advanced tuberculosis. But when applying immunizing measures they must be directed not only against the principal infecting organism but against all of the organisms that play a part in the infection. So in treating advanced cases of pulmonary tuberculosis it is necessary to give a vaccine containing the organisms causing the mixed infection in conjunction with the tubercle vaccine. I have often been surprised at the amount of relief this treatment gives in advanced cases of tuberculosis. We all know how hopeful these tubercular sufferers usually are and I can see absolutely no harm in stimulating that hope by making them feel more comfortable.

The therapeutic value of a remedy is often forcibly demonstrated by the results obtained under unfavorable conditions and this applies to the use of the non-virulent T. B. vaccine in advanced cases of tuberculosis.

The following case treated at the Detroit Tuberculosis Sanitarium offers a good illustration as to what can be accomplished in a badly advanced case. The particulars of this case were kindly furnished by Dr. F. E. Bowman.

Mr. F. H. Always had stomach trouble. Measles at age of 21. Mumps at age of 12. Pertussis at age of 5. Typhoid at age of 25. La Grippe at age of 30.

Normal weight, 165 lbs. Last day's work May 21, 1911, occupation, Ry. Conductor.

Date of first lung symptom, October, 1908. Loss of weight and often tired. Consulted Doctor for lung symptoms May, 1911. First examination sputum, August, 1911 which showed tubercle bacilli. Onset catarrhal. Had pleuritic pains on right side. Dyspnea dates since 1911. Hemoptysis—Blood streaks at times since 1911. Loss of strength marked since 1911. Chills, fever, night sweats during 1911,-12,-13. Had suffered with impared digestion for many years.

Physical examination, December 22, 1915, showed involvement of both lungs in all the lobes. Whole of right lung showed dullness. Fibrosis over each side—intensely so over right; marked retraction at right upper with vomica in right upper lobe. Examination showed far advanced chronic fibrosis. General impression of the patient, was low resistance, disseminated destruction, and poor expectoration.

Temperature: varied from 96 to 100.2 during December, 1915, from 96 to 99.6 during January, 1916, below normal during February, 1916, except 9th, 10th and 11th arose to 99.2 and on the 19th after .75 c. c. T. B. vaccine. During March, 1916 the temperature ran between 97 and 98.4. During April, 1916 the temperature ran between 96.4 and 98.6 —99 and 99.4 after vaccine inoculations.

Doses were given at first every other day, alternating the T. B. vaccine with a mixed vaccine.

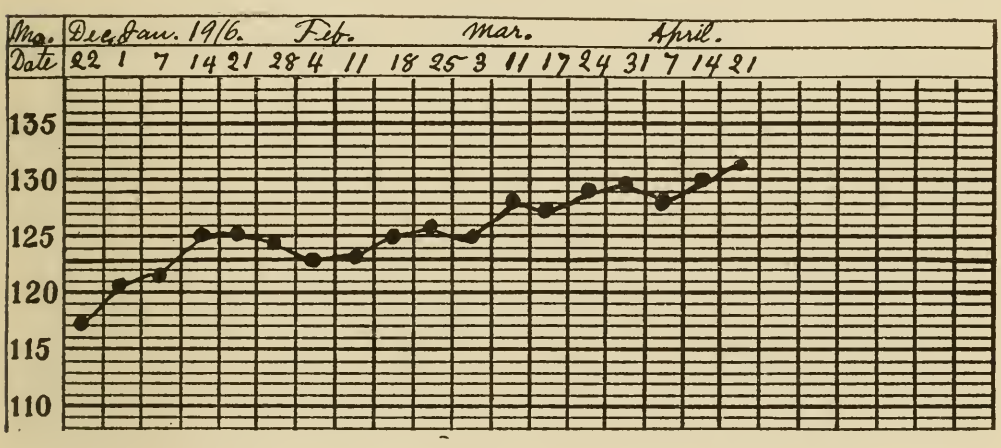
The T. B. vaccine 1,000,000,000 organisms per c. c. and the mixed vaccine contained streptococcus 60,000,000, pneumococcus 80,000,000, micrococcus catarrhalis 200,000,-

000 and staphylococcus aureus and albus each, 200,000,000 per c. c.

The minimum doses of the mixed vaccine were 0.3 c. c.; and of the T. B. vaccine 0.1 c. c. Maximum doses of the mixed vaccine were 0.9 c. c. and of the T. B. vaccine 0.8 c. c.

Increase in body weight is a good general indication of the progress a tubercular patient is making. The accompanying chart graphically illustrates the steady increase of body weight from the time vaccine treatment was instituted.

CHART SHOWING INCREASE IN BODY WEIGHT.



There is an apparent lessening in the amount of sputum and generally the patient feels better.

Dr. G. A. Persson of Mt. Clemens (Bacterial Therapist, May, 1916) reports extensive work on the blood picture in cases of tuberculosis after giving non-virulent tubercle bacillus vaccine and on account of the importance of this work I will reproduce it in toto:

"Studies of patient's blood in tuberculosis teaches lessons perhaps nowhere else to be learned. It reveals, at close range and in a graphic manner, a truly remarkable process. It unfolds to the astounded observer a struggle in which most extraordinary expenditure of energy takes place. It demonstrates Nature's method of warfare, "in the open" as well as "from protected positions." It brings home a

lesson of preparedness, from a biological standpoint, which should long remain clear in our memories. It makes the physician long for the dawn of that perfect day, when he can make the mechanism of immunization so respond to his administrations that susceptible patients may be protected against this dreaded disease. It sends a peaceful thought into the troubled minds of medical men who have borne with fortitude the painful realization that tuberculosis has, until very recent years, baffled their best efforts; because there stands today at command of the professional man, in scientific medicine, a potent remedial agent, in form of "Tubercular Bacterial Vaccines," which form a formidable weapon in his fight against an invading army of Koch's organism.

"The blood picture in tuberculosis varies with the stage, the acuteness and the complications.

"Erythrocytes may be found as low as 1,000,000 to c. m. m., but it is rarely they fall below 3,000,000 in uncomplicated cases. Patients under treatment often show a very high erythrocytic count. It is not uncommon to find 6,000,000 to the c. m. m. in such cases.

"In 155 patients at the Adirondack Cottage Sanitarium, a variation from 4,000,000 to 8,000,000 was observed.

"Haemoglobin is no less variable. Examination of 155 patients in the same institution showed the following figures—incipient male cases, 91%; advanced male cases, 90.4%; incipient female cases, 88.2%, and advanced female cases, 90.3%. In these cases a wide range was observed, in some instances as low as 65% and as high as 99%.

"Leucocytes. In the incipient stage the leucocyte count is sometimes very low. Often in these cases there is found 3,000 to 5,000 white cells, while in advanced cases 10,000 to 12,000 is very common.

"In the Adirondack Cottage Sanitarium, the leucocytes counted in 155 cases before breakfast, while fasting, showed an extraordinary wide range of variation, from 4,000 to 19,000, with a total average in incipient male cases of 9,950 —in advanced male cases 9,637—in incipient female cases 8,485, and in advanced female cases 9,744.

"According to Wright, Leishman and Douglas, the opsonic index in tubercular patients fluctuates widely, ranging from 0.3 to 1.8 or higher. This extreme fluctuation of the opsonic curve is not only characteristic in tuberculosis,

but also significant, because it represents a graphic illustration of the great struggle that takes place.

"Grace Calvert's observations on this point are summed up as follows:

'1. In slight early cases the index appears to be above normal.

'2. In acute cases the index fluctuates greatly from day to day.

'3. In chronic cases the index appears to be below normal.

'4. In Sanitarium cures the index appears to be variable.'

"Mekins and Wheeler, in their study of the opsonic index in tubercular patients under sanitarium treatment, found that when the opsonic index is constantly below normal, the disease progresses, while patients in which the opsonic index remains normal, usually show marked improvement, particularly when placed under hygienic and dietetic regime. A widely fluctuating opsonic index denotes autoinoculation and lowered resistance. The prognosis under this condition is usually grave.

"Our studies of the blood picture in tubercular patients has brought about the conclusion that while under a proper hygienic and dietetic regime there is usually an increase of haemoglobin and erythrocytes. This condition is not controlled directly by these measures, because very marked fluctuations are found, even when the patient observed a strict regime.

"What has been said about the haemoglobin and erythrocytes is also true of the tubercular opsonic index. The opsonic index in a tubercular patient is an ever changing scene, giving us little ground for prognosis in the case. This seeming unrest of the vital elements in the body fluids appear to us very significant, and any therapeutic measure, potent in causing a more constant state of these elements, would, in our opinion, be a valuable adjunct in the treatment of this class of cases.

"Tubercular vaccines, particularly of the 'non-virulent type,' have been found to exert some influences upon the blood picture in tubercular patients.

"To study the opsonic curve in patients receiving therapeutic doses of tubercular vaccines would lead to the conclusion that the immunizing mechanisms are, not only sup-

ported or sustained, but regulated or controlled. In support of this deduction I have the pleasure to offer the findings in several cases which have come under our observations.

"These cases have not been selected, but taken in routine from a series of 39 patients, all of which received practically the same treatment. The blood count was made under as near similar conditions as possible and the time selected was before breakfast while fasting—the dose of vaccine was 500,000,000 organisms every three days. On the intervening days 1 c.c. of a 5% solution of neucleinic acid was administered subcutaneously."

CASE No. 1

Day of Treatment	Opsonic Index	Hemoglobin	Red Blood Cells	White Blood Cells	Remarks
1	0.8	72%	3,296,520	9,300	FEMALE—Age 28 years. Tuberculosis was diagnosed nine months ago. Has lost some in weight. Patient has been under hygienic and dietetic regime. Has not received vaccine.
10	0.9	84%	4,382,600	9,800	
20	0.7	70%	2,824,900	9,570	
30	1.3	89%	4,926,300	9,262	
60	1.9	93%	5,265,871	9,200	

CASE No. 2

1	0.9	80%	3,121,384	8,200	FEMALE—Age 26 years. Two years tubercular. Sanitarium treatment for nine months and under hygienic and dietetic regime since diagnosis first was made. Vaccine treatment for two months. Last inoculation six months ago.
10	1.2	80%	3,621,896	8,384	
20	1.2	85%	4,268,341	8,631	
30	1.4	89%	4,639,400	8,718	
60	1.4	89%	4,627,321	8,724	

CASE No. 3

1	0.6	68%	2,829,300	10,200	MALE—Age 51 years. Advanced tuberculosis. Has lost 14 pounds in past 60 days. Coughs a great deal and expectoration profuse. T. B. numerous in sputum which contains streptococcus and pneumococcus in abundance.
10	0.8	70%	3,210,600	10,340	
20	0.8	70%	3,368,248	9,361	
30	1.2	84%	4,120,900	9,690	
60	1.2	88%	4,596,271	9,640	

CASE No. 4

1	1.2	78%	3,628,120	9,300	MALE—Age 56 years. Has had tuberculosis for several years. Been in sanitarium one year. Received T. B. vaccine one and a half years ago, during a period of 13 months. Sputum shows numerous T. B., some elastic tissue, blood and pus cells.
10	1.2	83%	3,910,450	9,800	
20	1.4	83%	4,967,391	9,624	
30	1.6	90%	4,732,900	9,432	
60	1.6	90%	5,380,973	9,381	

CASE No. 5

Day of Treatment	Opsonic Index	Hemoglobin	Red Blood Cells	White Blood Cells	Remarks
1	1.3	84%	4,287,200	12,200	MALE—Age 28 years. Coughing for three months. Expectorates only in morning. T. B. discovered in sputum two months ago. Patient has lost considerable in weight during past 60 days. Has never received any vaccine treatment.
10	0.8	92%	4,896,300	11,890	
20	1.4	90%	5,732,810	11,436	
30	1.3	94%	5,462,891	10,326	
60	1.9	94%	5,458,321	9,634	

CASE No. 6

1	1.4	76%	3,842,621	7,390	MALE—Age 48 years. Advanced case. Has received vaccine treatment on three previous occasions for periods of time ranging from three weeks to four months. Streptococcus and pneumococcus very abundant in sputum. T. B. moderately numerous.
10	0.7	84%	4,281,436	7,821	
20	1.6	89%	4,832,691	7,850	
30	1.6	92%	5,386,200	7,900	
60	1.9	92%	5,325,836	7,900	

CASE No. 7

1	1.0	72%	3,628,391	10,266	FEMALE—Age 28 years. Never received any vaccine treatment. Diagnosis of tuberculosis was made seven months ago. Patient has been on hygienic and dietetic treatment for four months. Condition unchanged.
10	0.8	83%	3,946,821	10,931	
20	1.4	89%	4,126,506	9,920	
30	1.7	94%	4,739,260	9,732	
60	1.7	95%	4,763,240	9,500	

CASE No. 8

1	1.2	68%	3,196,321	6,280	FEMALE—Age 42 years. Advanced case. Received sanitation treatment for about a year followed by hygienic and dietetic treatment at home. Patient has received vaccine treatment during a short period. Last inoculation about three months ago.
10	1.2	72%	3,629,400	6,890	
20	1.4	76%	3,729,250	6,875	
30	1.4	88%	4,593,200	6,900	
60	1.8	88%	4,573,200	6,900	

CASE No. 9

1	0.8	78%	3,292,600	7,320	MALE—Age 30 years. Tuberculosis for three years. Spent two years in the West. Has been under observation of medical men receiving hygienic and dietetic treatment. Had tubercular vaccine for a period of three months about two years ago.
10	0.8	80%	3,789,230	7,500	
20	1.2	80%	3,962,450	7,550	
30	1.2	88%	4,100,260	7,500	
60	1.4	90%	4,290,300	7,200	

CASE No. 10

Day of Treatment	Opsonic Index	Hemo-globin	Red Blood Cells	White Blood Cells	Remarks
1	1.2	87%	4,200,561	9,210	FEMALE—Age 21 years. Mild case of about four months. T. B. procured but few in number. Cough slight and expectoration moderate. Slight even temperature and night sweat. Some loss in weight. Patient has been under hygienic and dietetic regime but has not received vaccine treatment.
10	0.9	95%	5,283,300	9,340	
20	1.4	95%	5,393,200	9,250	
30	1.4	95%	5,300,250	9,000	
60	1.2	95%	5,420,381	9,000	

CASE No. 11

1	1.2	66%	2,832,750	11,220	MALE—Age 28 years. Very emaciated. Coughs a great deal. Expectoration very profuse, streaked with blood. Diagnosis of T. B. seven months ago. Has lost much in weight. Has been under hygienic and dietetic treatment. No vaccine.
10	1.4	79%	3,426,200	11,000	
20	1.4	84%	3,591,275	10,830	
30	1.4	85%	4,297,350	10,720	
60	1.4	89%	4,250,387	10,930	

CASE No. 12

1	1.2	70%	3,126,391	6,210	MALE—Age 48 years. Advanced case. Has been under hygienic and dietetic regime for two years. Received vaccine for short periods several times, the last dose about four months ago.
10	1.0	74%	3,492,500	6,834	
20	1.4	80%	3,960,780	6,720	
30	1.8	80%	4,000,590	6,890	
60	1.8	82%	4,198,675	6,900	

CASE No. 13

1	1.1	78%	3,482,600	10,200	FEMALE—Age 48 years. Advanced case. Has received sanitation, hygienic and dietetic treatment. Vaccine for a period of two months, last inoculation about six months ago.
10	0.7	86%	3,596,550	10,200	
20	1.3	86%	4,287,100	9,620	
30	1.4	90%	4,628,650	9,890	
60	1.4	90%	4,593,200	9,524	

CASE No. 14

1	1.3	82%	3,892,600	9,000	FEMALE—Age 32 years. Tuberculosis diagnosed nine months ago. Under dietetic and hygienic regime. From this time received vaccine for two months at onset.
10	0.9	85%	4,296,700	9,200	
20	1.4	85%	4,389,100	9,280	
30	1.5	90%	4,962,820	9,600	
60	1.9	90%	4,832,900	9,721	

CASE No. 15

Day of Treatment	Opsonic Index	Hemoglobin	Red Blood Cells	White Blood Cells	Remarks
1	1.1	85%	4,286,250	12,300	MALE—Age 28 years. Diagnosis of T. B. four months ago. Patient on hygienic and dietetic regime. Lived out of doors under ideal conditions.
10	0.9	85%	4,399,400	11,350	
20	1.4	92%	4,628,300	11,000	
30	1.4	96%	4,928,550	11,200	
60	1.8	96%	4,826,300	10,150	

CASE No. 16

1	1.0	73%	3,893,200	8,900	MALE—Age 42 years. Advanced case. Patient has been under hygienic and dietetic regime for two years. Unfortunately financial conditions prevented him from taking advantage of all the benefits such regime affords a patient. Had vaccine for a period of three months, last inoculation 42 days ago.
10	0.7	78%	3,872,930	8,720	
20	1.3	82%	4,320,500	8,930	
30	1.3	90%	4,500,000	8,640	
60	1.4	90%	4,386,200	8,600	

CASE No. 17

1	0.9	80%	4,127,390	9,300	MALE—Age 36 years. Tuberculosis for three years. Lives on a farm. Has been under hygienic and dietetic regime for two and a half years. Received daily inoculation of nucleinic acid—1 cc. $5\frac{5}{16}$ dilatuion in physiological salt solution. Last inoculation 30 days ago.
10	0.7	80%	4,596,300	9,000	
20	1.2	84%	4,683,798	9,280	
30	1.5	85%	4,590,600	10,000	
60	1.5	90%	4,839,250	9,283	

CASE No. 18

1	1.3	95%	4,286,531	10,300	MALE—Age 29 years. Diagnosis of tuberculosis seven months ago. Vaccine for 30 days. Last inoculation two months ago. Patient has never been on any strict regime.
10	1.5	84%	4,683,200	10,280	
20	0.9	75%	4,129,387	10,300	
30	1.5	90%	4,783,800	10,480	
60	1.6	90%	4,983,764	10,590	

"It has been said, I believe, about tuberculosis, that this malignant process in the human body may fittingly be called "a biologic war." Viewing the pathological conditions from such standpoints, we see before us a great struggle for supremacy in which the invading foe cannot be compromised or arbitrated with. From the onset it is a "fight to the finish," and it therefore becomes necessary for the human organisms to bring into action all her defending forces as early as possible.

"This struggle is peculiarly typified in our modern mili-

tary stratagem. Today, two opposing armies on the battlefield can, by the use of protected intrenchments, get into very close range of each other and by virtue of these positions, a sweeping advance on either side is well guarded against.

"When a drive is planned, the heavy artillery from the rear is brought into play to bombard the enemies' protected trenches and cause as much destruction as possible. Under cover of this artillery fire, the occupants of the trenches make their attack.

"Let us see how such tactics apply to tuberculosis.

"The tubercular organisms succeed, perhaps better than most of the pathogenic germs with which we have to deal, in securing protection and cultivating themselves in positions difficult to attack.

"For example: A tubercular nodule is in itself a miniature fort behind the protecting walls of which tubercle bacilli are comparatively safe at least from attacks by the leucocytes.

"To capture these intrenched organisms, it becomes necessary for Nature's proteolytic forces to use the same military strategy as we have just outlined.

The heavy artillery which, in the above illustration, played such an important part making a successful drive on the battlefield, is here represented by the various ferments and enzymes that prepare the offending organisms for a successful attack by the leucocytes. This biological process has been called in broad terms "stimulation of the immunizing mechanism," which is registered graphically through the opsonic index.

"The tubercular opsonic index is raised in nearly all cases through inoculations of suitable tubercular bacterial vaccines. This has been the experience of many investigators. It would, therefore, be safely within the limits of conservatism to form the conclusion that in combating tuberculosis, a suitable tubercular vaccine is the real heavy artillery by means of which an attack of Nature's forces are facilitated.

"It is not long ago since tuberculosis was regarded by medical men as a field in which their labors were all in vain. Today, however, we do not hesitate to speak of it with comparative optimism and confidence as to results from proper treatment. Why this transformation of medical

opinion? Nothing new regarding its etiology or pathology has been discovered nor have we happened to hit upon a more efficient dietetic and hygienic regime. Even our store of therapeutic application in the treatment of tuberculosis has not, during recent years, been enriched with the exception of a proper administration of suitable bacterial tubercle vaccine. If we have ground for our optimism, it appears that tubercle vaccine is really responsible for such confidence. Let it, therefore, not be considered as a mere experiment or as a last resort therapeutic application to use a suitable tubercle vaccine in all cases of tuberculosis."

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